

Supporting Information

Pd-Catalyzed C–H Halogenation of Indolines and Tetrahydroquinolines with Removable Directing Group

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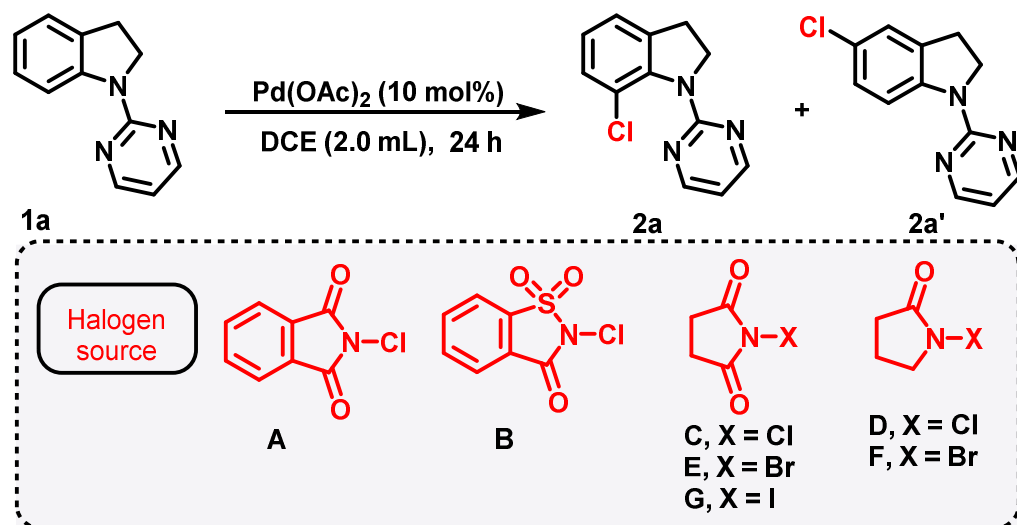
General Information

Reactions were performed using borosil sealed tube vial. Column chromatography was done in 60Å-120Å silica gel of Merck Company. All solvents were distilled for purification in column chromatography. All spectra ^1H NMR, ^{13}C NMR, recorded on Bruker AV 400 MHz spectrometer in CDCl_3 using as internal standards the residual CHCl_3 for ^1H NMR ($\delta = 7.26$ ppm respectively) and the deuterated solvent signal for ^{13}C NMR ($\delta = 77.00$ ppm respectively). HRMS analysis was performed using Q-TOF mass spectrometer of the SAIF division in CSIR-CDRI Lucknow. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublet, m = multiplet. Coupling constants, J , were reported in hertz (Hz). HRMS analysis was performed using Q-TOF mass spectrometer of the SAIF Division in CSIR-CDRI Lucknow. IR analysis was also performed in SAIF Division. Reagents and starting materials were purchased from Aldrich, Alfa Aesar and other commercial sources and used without further purification unless otherwise noted.

Synthesis of precursors: The indoline pyrimidine derivatives (**1a-1m**)¹⁻³, quinoline pyrimidine (**5a-5h**)⁴, *N*-(4-aminopentyl)-4-phenylbutanamide⁶ and *N*-bromopyrrolidinone (**F**)⁸ as the precursors for the starting were prepared via reported method.

Optimization Studies

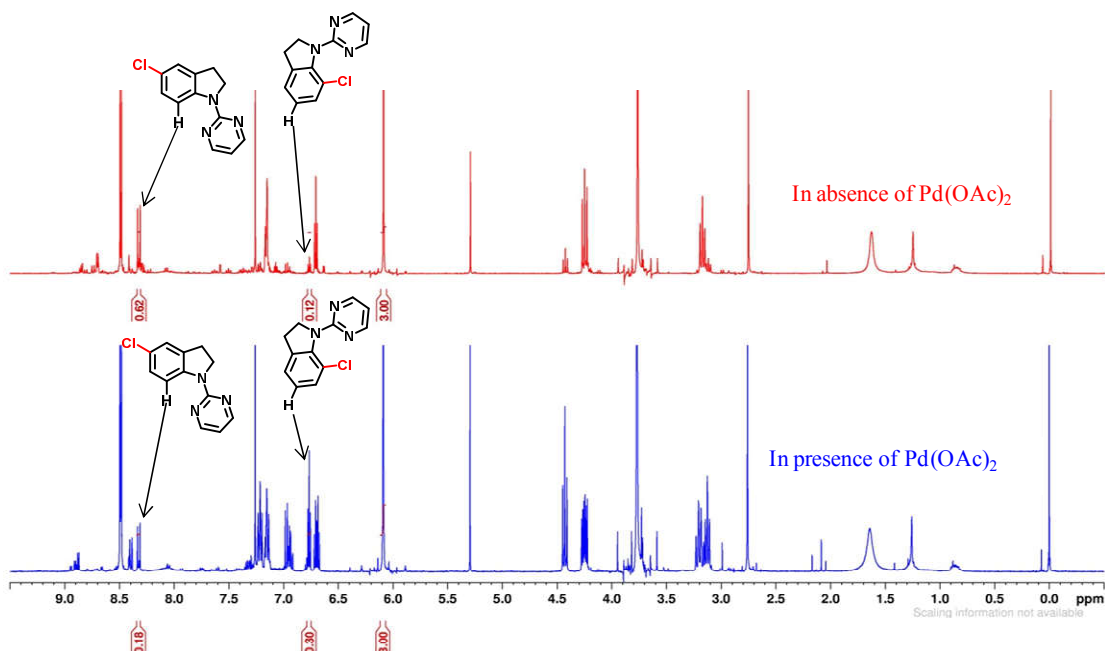
Table S1. Screening of Chlorinating reagent for C7 Chlorination:



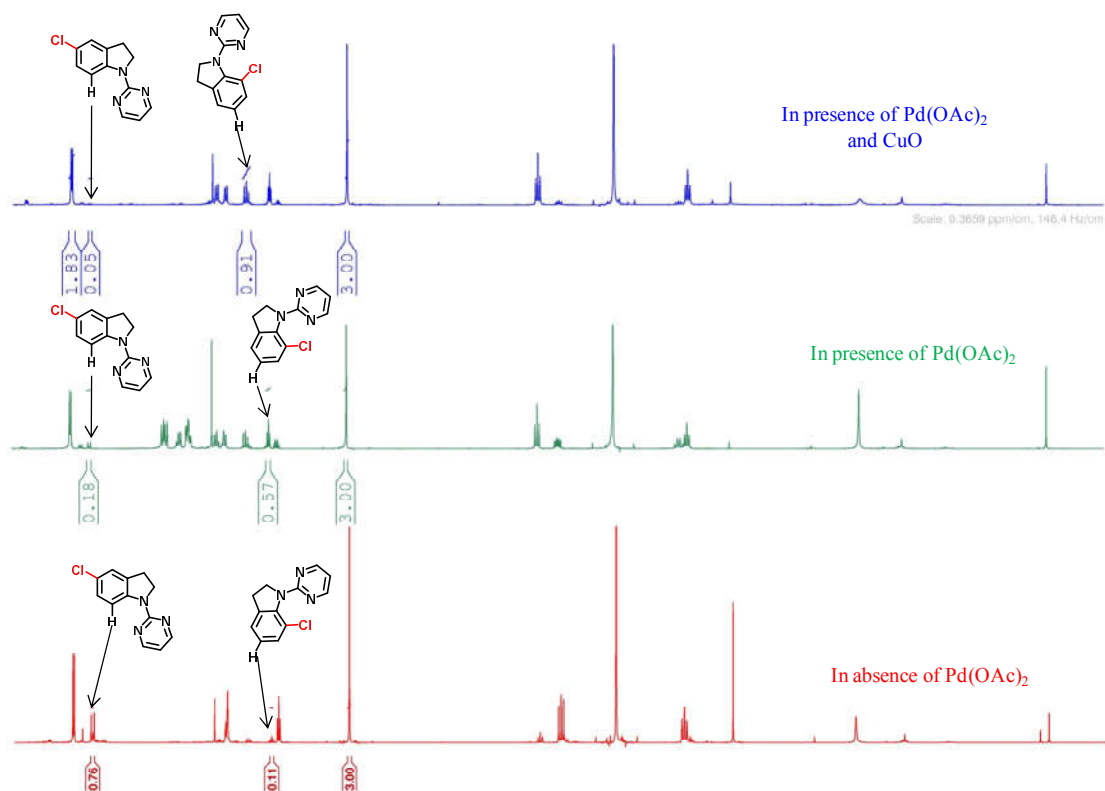
Entry	Catalyst (mol%)	Reagent	Oxidant (equiv)	Temp (°C)	Yield% (2a/2a')
1	$\text{Pd}(\text{OAc})_2$ (10)	A	--	rt	--
2	--	A	--	rt	14/69
3	$\text{Pd}(\text{OAc})_2$ (10)	B	--	rt	26/63
4	--	B	--	rt	11/66
5	$\text{Pd}(\text{OAc})_2$ (10)	C	--	rt	trace
6	--	C	--	rt	--
7	$\text{Pd}(\text{OAc})_2$ (10)	D	--	rt	--
8	--	D	--	rt	trace
9	$\text{Pd}(\text{OAc})_2$ (10)	C	CuO (1.0)	rt	17/5
10	$\text{Pd}(\text{OTs})_2(\text{CH}_3\text{CN})_2$ (10)	C	CuO (1.0)	rt	traces
11	$\text{Pd}(\text{TFA})_2$ (10)	C	CuO (1.0)	rt	21/3
12	$\text{Pd}(\text{OAc})_2$ (10)	C	--	45	trace

13	--	C	--	45	--
14	Pd(OAc) ₂ (10)	D	--	45	trace
15	--	D	--	45	--
16	Pd(OAc) ₂ (10)	C	--	70	30/18
17	--	C	--	70	12/62
18	Pd(OAc) ₂ (10)	C	--	90	57/18
19	--	C	--	90	11/76
20	Pd(OAc)₂ (10)	C	CuO (1.0)	90	91/05
21	Pd (OTs) ₂ (CH ₃ CN) ₂	C	CuO (1.0)	90	80/18
22	Pd (TFA) ₂	C	CuO (1.0)	90	89/8
23	Pd(OAc) ₂ (10)	C	CuO (1.0)	80	71/09
24	Pd(OAc) ₂ (10)	D	CuO (1.0)	90	88/10
25	--	C	CuO (1.0)	90	8/67
26	Pd(OAc) ₂ (10)	D	--	90	47/19
27	--	D	--	90	12/81
28	--	D	CuO (1.0)	90	10/44

Reaction Conditions: 0.25 mmol of **indoline**, 1.2 equiv of **halogenating source**, 2 mL of solvent, nmr yield using 1,3,5-trimethoxybenzene 0.25 mmol internal standard.

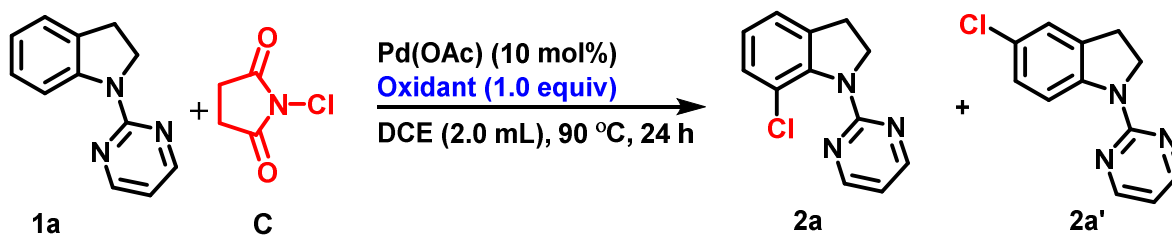


Crude ¹H NMR spectra of entry 16 and 17 **Table S1** at 70 °C using 1,3,5-trimethoxybenzene 1 equiv internal standard (400 MHz, CDCl₃)



Crude ¹H NMR spectra of entry 18, 19 and 20 **Table S1** at 90 °C using 1,3,5-trimethoxybenzene 1 equiv internal standard (400 MHz, CDCl₃)

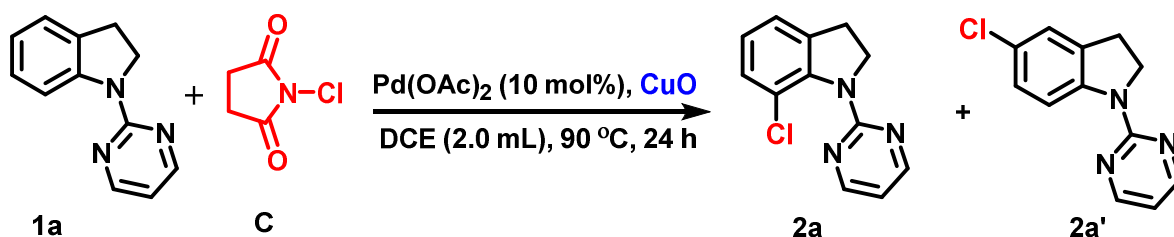
Table S2. Screening of Oxidant for C7 Chlorination:



Entry	Oxidant (equiv)	Yield% (2a/2a')
1	Cu ₂ O (1.0)	81/00
2	Cu(TFA) ₂ (1.0)	86/9
3	Cu(OAc) ₂ (1.0)	50/00
4	K ₂ S ₂ O ₈ (1.0)	27/34
5	AgTFA (1.0)	traces

Reaction Conditions: 0.25 mmol of indoline, 1.2 equiv of C, 2 mL of solvent, nmr yield using 1,3,5-trimethoxybenzene 0.25 mmol internal standard.

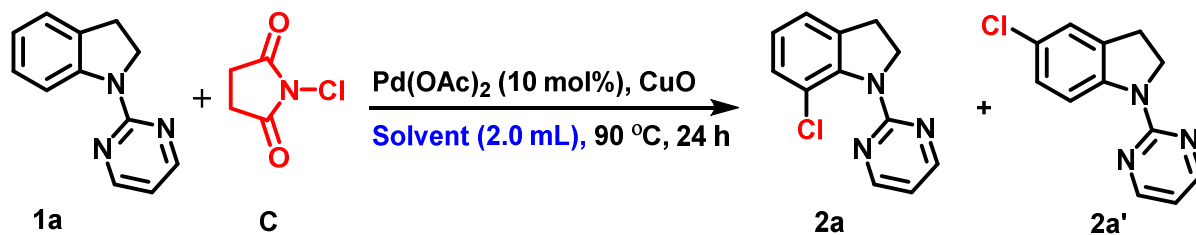
Table S3. Screening amount of CuO for C7 Chlorination:



Entry	CuO (equiv)	Yield% (2a/2a')
1	CuO (0.2)	56/18
2	CuO (0.5)	59/20
3	CuO (0.7)	68/18
4	CuO (1.2)	82/07
5	CuO (1.5)	71/22

Reaction Conditions: 0.25 mmol of indoline, 1.2 equiv of C, 2 mL of solvent, nmr yield using 1,3,5-trimethoxybenzene 0.25 mmol internal standard.

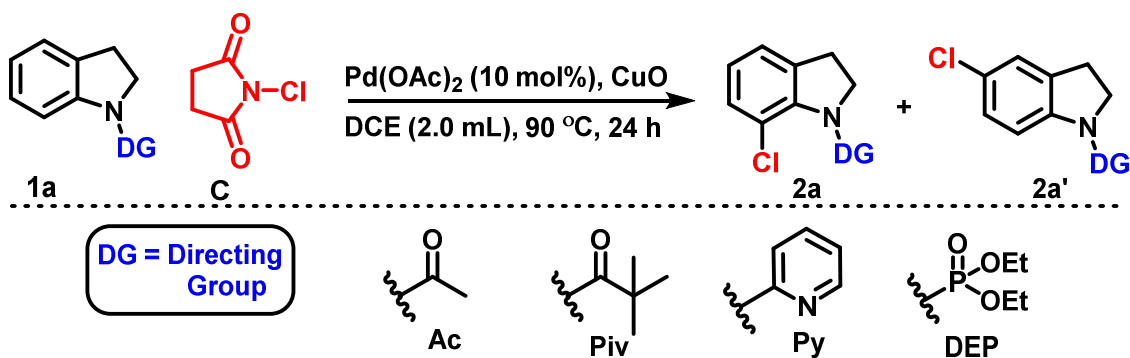
Table S4. Screening of Solvent for C7 Chlorination:



Entry	Solvent	Yield% (2a/2a')
1	Acetonitrile	35/00
2	Mesitylene	traces
3	Benzonitrile	43/00
4	DMF	18/00
5	DMSO	--
6	DMA	72/00

Reaction Conditions: 0.25 mmol of indoline, 1.2 equiv of C, 2 mL of solvent, nmr yield using 1,3,5-trimethoxybenzene 0.25 mmol internal standard.

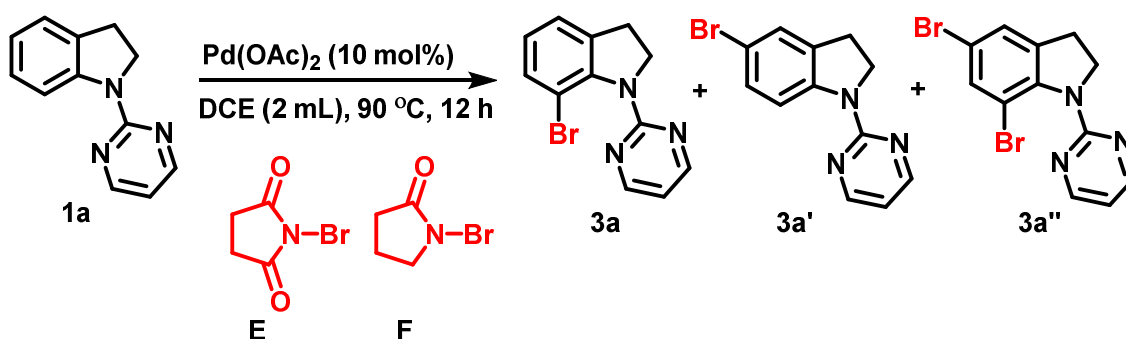
Table S5. Screening of Directing group for C7 Chlorination:



Entry	DG	Yield% (2a/2a')
1	Ac	--
2	Piv	trace
3	Py	25/--
4	DEP	--/65

Reaction Conditions: 0.25 mmol of indoline, 1.2 equiv of C, 2 mL of solvent, nmr yield using 1,3,5-trimethoxybenzene 0.25 mmol internal standard.

Table S6. Optimization condition for C7 Bromination:

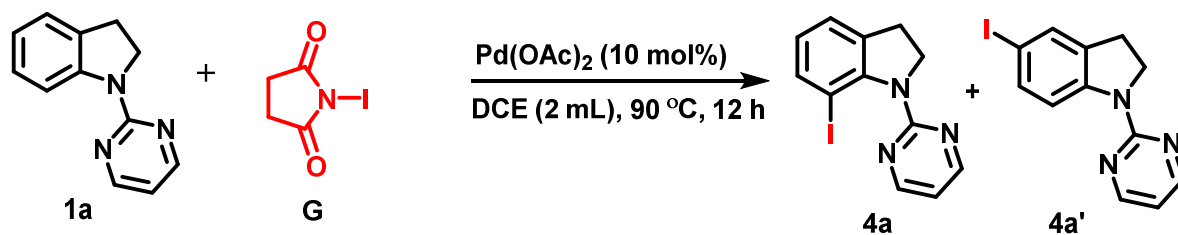


Entry	Reagent (equiv)	Oxidant (equiv)	Yield% (3a/3a'/3a'')
1	E (1.2)	--	--/60/--
2	F (1.2)	--	19/45/14
3	E (1.2)	CuO (1.0)	--/54/--

5	F (1.2)	CuO (1.0)	38/8/9
6	F (1.2)	CuO (2.0)	54/16/10
7	F (1.0)	CuO (2.0)	55/5/--

Reaction Conditions: 0.25 mmol of indoline, 2 mL of solvent, nmr yield using 1,3,5-trimethoxybenzene 0.25 mmol internal standard.

Table S7. Optimization condition for C7 Iodination:



Entry	Reagent (equiv)	Oxidant (equiv)	Yield% (4a/4a')
1	G (1.0)	CuO (2.0)	00/55

Reaction Conditions: 0.25 mmol of indoline, 2 mL of solvent, nmr yield using 1,3,5-trimethoxybenzene 0.25 mmol internal standard.

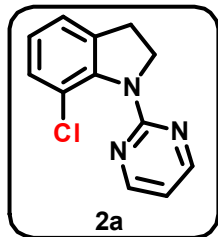
General procedure for the synthesis of Chlorination (A): To a solution of indoline pyrimidine (0.25 mmol) in DCE (2 mL), Pd(OAc)₂ (5.7 mg, 10 mol%), C (40.6 mg, 1.2 equiv) and CuO (20 mg, 1 equiv) was added in a sealed tube vial and the reaction mixture was kept in preheated oil bath at 90 °C for 24 hours. After completion of the reaction, the reaction mixture was directly subjected to column chromatography, which yielded the corresponding chlorinated product.

General procedure for the synthesis of bromination (B): To a solution of indoline pyrimidine (0.25 mmol) in DCE (2 mL), Pd(OAc)₂ (5.7 mg, 10 mol%), F (41 mg, 1 equiv) and CuO (40 mg, 2 equiv) was added in a sealed tube vial and the reaction mixture was kept in preheated oil bath at 90 °C for 12 hours. After completion of the reaction, the reaction mixture was directly subjected to column chromatography, which yielded the corresponding chlorinated product.

Note: In case of 2j Pd(TFA)₂ (10 mol%) was used.

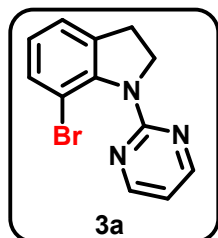
Synthesis and characterization of Halogenated compounds:

7-chloro-1-(pyrimidin-2-yl)indoline (2a): **2a** was prepared according to general procedure (A) using indoline pyrimidine **1a** (50 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2 equiv).



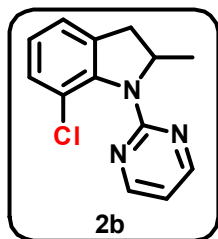
The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **2a** (50 mg, 85%) as a white solid. **R_f**: 0.60 (silica gel, 20% EtOAc/Hexane); **M. P.**: 118-123 °C; **IR (in CHCl₃, cm⁻¹):** ν_{max} : 3018, 1577, 1555, 1461, 1426, 1214, 1135, 1050, 901, 742; **¹H NMR (400 MHz, CDCl₃):** δ 8.48 (d, J = 4.8 Hz, 2H), 7.22 (dd, J = 8.0 Hz, 0.7 Hz, 1H), 7.14 (dd, J = 7.3 Hz, 1.0 Hz, 1H), 6.96 (t, J = 7.7 Hz, 1H), 6.76 (t, J = 4.8 Hz, 1H), 4.42 (t, J = 8.0 Hz, 2H), 3.12 (t, J = 7.6 Hz, 2H); **¹³C NMR (100 MHz, CDCl₃):** δ 160.8, 157.6, 141.8, 137.1, 129.0, 124.7, 123.9, 123.0, 113.2, 53.8, 30.2; **HRMS (ESI) m/z:** [M + H]⁺ Calcd for C₁₂H₁₁ClN₃ 232.0636; Found 232.0633.

7-bromo-1-(pyrimidin-2-yl)indoline (3a): **3a** was prepared according to general procedure (B) using indoline pyrimidine **1a** (50 mg, 0.25 mmol), halogenating source **F** (41 mg, 1.0 equiv). The



crude reaction mixture was purified by column chromatography using 20% EtOAc/Hexane afforded **3a** (34 mg, 50%) as a white solid. **R_f**: 0.41 (silica gel, 20% EtOAc/Hexane); **M. P.**: 123-127 °C; **IR (in CHCl₃, cm⁻¹):** ν_{max} : 2953, 1573, 1556, 1461, 1350, 1224, 1198, 1117, 1059, 992; **¹H NMR (400 MHz, CDCl₃):** δ 8.49 (d, J = 4.8 Hz, 2H), 7.40 (dd, J = 8.0 Hz, 0.8 Hz, 1H), 7.19 (dd, J = 7.3 Hz, 1.0 Hz, 1H), 6.89 (t, J = 7.8 Hz, 1H), 6.77 (t, J = 4.8 Hz, 1H), 4.43 (t, J = 7.9 Hz, 2H), 3.13 (t, J = 7.6 Hz, 2H); **¹³C NMR (100 MHz, CDCl₃):** δ 160.6, 157.4, 143.5, 137.2, 131.9, 124.8, 123.5, 113.2, 112.8, 53.8, 30.3; **HRMS (ESI) m/z:** [M + H]⁺ Calcd for C₁₂H₁₁BrN₃ 276.0131; Found 276.0132.

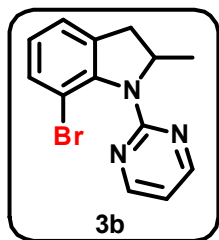
7-chloro-2-methyl-1-(pyrimidin-2-yl)indoline (2b): **2b** was prepared according to general procedure (A) using indoline pyrimidine **1b** (53 mg, 0.25 mmol), halogenating source **C** (41 mg,



1.2 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **2b** (55 mg, 88%) as a white solid. **R_f**: 0.50 (silica gel, 20% EtOAc/Hexane); **M. P.**: 108-113 °C; **IR (in CHCl₃, cm⁻¹):** ν_{max} : 3019, 1579, 1554, 1461, 1428, 1279, 1214, 1137, 997,

743; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 8.47 (d, $J = 4.8$ Hz, 2H), 7.22 (d, $J = 8.0$ Hz, 1H), 7.13 (d, $J = 7.3$ Hz, 1H), 6.97 (t, $J = 7.7$ Hz, 1H), 6.75 (t, $J = 4.8$ Hz, 1H), 4.95–4.85 (m, 1H), 3.52 (dd, $J = 15.4$ Hz, 8.5 Hz, 1H), 2.55 (d, $J = 15.4$ Hz, 1H) 1.42 (d, $J = 6.6$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 160.5, 157.6, 140.4, 135.8, 129.1, 124.6, 124.3, 123.5, 113.3, 61.5, 37.4, 21.7; **HRMS (ESI)** m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{13}\text{ClN}_3$ 246.0793; Found 246.0810.

7-bromo-2-methyl-1-(pyrimidin-2-yl)indoline (3b): **3b** was prepared according to general procedure (B) using indoline pyrimidine **1b** (53 mg, 0.25 mmol), halogenating source **F** (41 mg,

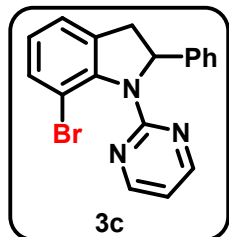


1.0 equiv). The crude reaction mixture was purified by column chromatography using 7% EtOAc/Hexane afforded **3b** (46 mg, 63%) as a white solid. **R_f**: 0.61 (silica gel, 20% EtOAc/Hexane); **M. P.**: 110–115 °C; **IR** (in CHCl_3 , cm^{-1}): ν_{max} ; 2984, 1576, 1555, 1427, 1278, 1226, 1112, 1052, 978, 745; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 8.48 (d, $J = 4.8$ Hz, 2H), 7.41 (d, $J = 8.0$

Hz, 1H), 7.18 (dd, $J = 7.3$ Hz, 0.7 Hz, 1H), 6.89 (t, $J = 7.7$ Hz, 1H), 6.75 (t, $J = 4.8$ Hz, 1H), 4.94–4.86 (m, 1H), 3.53 (dd, $J = 15.5$ Hz, 8.3 Hz, 1H), 2.55 (d, $J = 15.5$ Hz, 1H) 1.42 (d, $J = 6.7$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 160.3, 157.4, 135.9, 134.0, 131.9, 124.7, 124.0, 113.3, 113.2, 61.4, 37.2, 21.5; **HRMS (ESI)** m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{13}\text{BrN}_3$ 290.0287; Found 290.0290.

7-chloro-2-phenyl-1-(pyrimidin-2-yl)indoline (2c): **2c** was prepared according to general procedure (A) using indoline pyrimidine **1c** (69 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **2c** (70 mg, 89%) as a white solid. **R_f**: 0.50 (silica gel, 20% EtOAc/Hexane); **M. P.**: 152–157 °C; **IR** (in CHCl_3 , cm^{-1}): ν_{max} ; 3018, 2926, 1578, 1556, 1461, 1425, 1290, 1214, 1056, 899; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 8.47 (d, $J = 4.8$ Hz, 2H), 7.39–7.34 (m, 2H), 7.33–7.18 (m, 4H) 7.06 (dd, $J = 7.3$ Hz, 0.5 Hz, 1H), 6.96 (t, $J = 7.5$ Hz, 1H), 6.76 (t, $J = 4.8$ Hz, 1H), 5.91 (d, $J = 8.8$ Hz, 1H), 3.90 (dd, $J = 15.5$ Hz, 9.3 Hz, 1H), 2.99 (d, $J = 15.5$ Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 160.4, 157.6, 142.8, 141.2, 135.0, 128.9, 128.5, 127.1, 125.4, 124.9, 124.0, 123.1, 113.4, 67.4, 39.1; **HRMS (ESI)** m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{18}\text{H}_{15}\text{ClN}_3$ 308.0949; Found 308.0962.

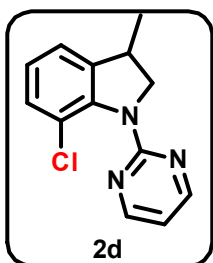
7-bromo-2-phenyl-1-(pyrimidin-2-yl)indoline (3c): **3c** was prepared according to general procedure (B) using indoline pyrimidine **1c** (69 mg, 0.25 mmol), halogenating source **F** (41 mg,



1.0 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **3c** (56 mg, 63%) as a white solid. **R_f**: 0.43 (silica gel, 20% EtOAc/Hexane); **M. P.**: 192-197 °C; **IR (in CHCl₃, cm⁻¹):** ν_{\max} ; 3012, 1576, 1556, 1556, 1459, 1425, 1214, 1052, 876, 743; **¹H NMR (400 MHz, CDCl₃):** δ 8.49 (d, J = 4.8 Hz, 2H), 7.44 (d, J

= 8.0 Hz, 1H), 7.40–7.35 (m, 2H), 7.34–7.28 (m, 2H), 7.25–7.20 (m, 1H), 7.11 (d, J = 7.3 Hz, 1H), 6.89 (t, J = 7.6 Hz, 1H), 6.78 (t, J = 4.8 Hz, 1H), 5.93 (d, J = 8.7 Hz, 1H), 3.93 (dd, J = 15.6 Hz, 9.0 Hz, 1H), 3.00 (d, J = 15.7 Hz, 1H); **¹³C NMR (100 MHz, CDCl₃):** δ 160.3, 157.6, 143.0, 142.9, 135.2, 131.9, 128.6, 127.2, 125.4, 125.3, 123.8, 113.6, 113.0, 67.5, 39.3; **HRMS (ESI) m/z:** [M + H]⁺ Calcd for C₁₈H₁₅BrN₃ 352.0444, Found 352.0442.

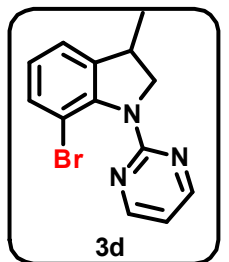
7-chloro-3-methyl-1-(pyrimidin-2-yl)indoline (2d): **2d** was prepared according to general



procedure (A) using indoline pyrimidine **1d** (53 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **2d** (45 mg, 72%) as a colourless oil. **R_f**: 0.65 (silica gel, 20% EtOAc/Hexane); **IR (in CHCl₃, cm⁻¹):** ν_{\max} ; 3025, 1670, 1327, 1265, 1225, 1030, 840; **¹H**

NMR (400 MHz, CDCl₃): δ 8.48 (d, J = 4.8 Hz, 2H), 7.23 (dt, J = 7.8 Hz, 0.8 Hz, 1H), 7.09 (dt, J = 7.3 Hz, 1.0 Hz, 1H), 6.99 (t, J = 7.5 Hz, 1H), 6.75 (t, J = 4.8 Hz, 1H), 4.59 (dd, J = 11.0 Hz, 8.1 Hz, 1H), 3.93 (dd, J = 11.0 Hz, 7.5 Hz, 1H), 3.51–3.39 (m, 1H) 1.28 (d, J = 6.9 Hz, 3H); **¹³C NMR (100 MHz, CDCl₃):** δ 160.7, 157.5, 142.0, 141.3, 128.9, 124.7, 123.6, 121.2, 113.0, 61.4, 36.8, 18.5; **HRMS (ESI) m/z:** [M + H]⁺ Calcd for C₁₃H₁₃ClN₃ 246.0793; Found 246.0796.

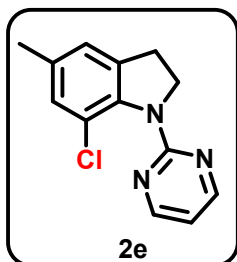
7-bromo-3-methyl-1-(pyrimidin-2-yl)indoline (3d): **3d** was prepared according to general procedure (B) using indoline pyrimidine **1d** (53 mg, 0.25 mmol), halogenating source **F** (41 mg,



1.0 equiv). The crude reaction mixture was purified by column chromatography using 7% EtOAc/Hexane afforded **3d** (39 mg, 54%) as a white solid. **R_f**: 0.50 (silica gel, 20% EtOAc/Hexane); **M. P.**: 88-93 °C; **IR (in CHCl₃, cm⁻¹):** ν_{\max} ; 2965, 1576, 1556, 1454, 1425, 1282, 1225, 1050, 990; **¹H NMR (400 MHz, CDCl₃):** δ 8.42 (d, J = 4.8 Hz, 2H), 7.34 (dt, J = 8.0 Hz,

0.9 Hz, 1H), 7.07 (dt, $J = 7.3$ Hz, 1.1 Hz, 1H), 6.85 (t, $J = 7.7$ Hz, 1H), 6.69 (t, $J = 4.8$ Hz, 1H), 4.53 (dd, $J = 11.0$ Hz, 8.0 Hz, 1H), 3.86 (dd, $J = 11.1$ Hz, 7.4 Hz, 1H), 3.46–3.33 (m, 1H), 1.20 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 160.8, 157.5, 143.2, 142.3, 131.9, 125.0, 122.2, 113.2, 112.7, 61.5, 37.5, 18.5; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{13}\text{BrN}_3$ 290.0287; Found 290.0291.

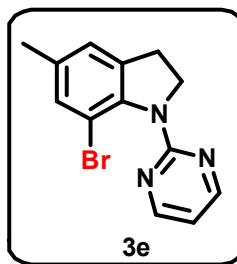
7-chloro-5-methyl-1-(pyrimidin-2-yl)indoline (2e): 2e was prepared according to general



procedure (A) using indoline pyrimidine **1e** (53 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **2e** (43 mg, 69%) as a white solid. **R_f**: 0.51 (silica gel, 20% EtOAc/Hexane);

M. P.: 100–105 °C; **IR** (in CHCl_3 , cm^{-1}): ν_{max} ; 3015, 1770, 1527, 1365, 1250, 1130, 1040, 870; ^1H NMR (400 MHz, CDCl_3): δ 8.46 (d, $J = 4.8$ Hz, 2H), 7.04 (s, 1H), 6.96 (s, 1H), 6.73 (t, $J = 4.8$ Hz, 1H), 4.40 (t, $J = 7.7$ Hz, 2H), 3.07 (t, $J = 8.0$ Hz, 2H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 161.0, 157.6, 139.4, 137.0, 134.9, 129.2, 123.9, 123.5, 113.0, 53.9, 30.3, 20.9; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{13}\text{ClN}_3$ 246.0793; Found 246.0793.

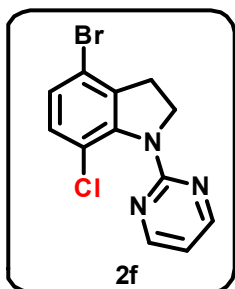
7-bromo-5-methyl-1-(pyrimidin-2-yl)indoline (3e): 3e was prepared according to general



procedure (B) using indoline pyrimidine **1e** (53 mg, 0.25 mmol), halogenating source **F** (41 mg, 1.0 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **3e** (41 mg, 55%) as a white solid. **R_f**: 0.47 (silica gel, 20% EtOAc/Hexane); **M. P.:** 93–98 °C; **IR** (in CHCl_3 , cm^{-1}): ν_{max} ; 3018, 1578,

1554, 1471, 1407, 1214, 1110, 1048, 853; ^1H NMR (400 MHz, CDCl_3): δ 8.47 (d, $J = 4.8$ Hz, 2H), 7.24–7.21 (m, 1H), 7.00 (s, 1H), 6.74 (t, $J = 4.8$ Hz, 1H), 4.41 (t, $J = 7.9$ Hz, 2H), 3.07 (t, $J = 7.7$ Hz, 2H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 160.8, 157.4, 141.1, 137.1, 135.0, 132.0, 124.4, 113.0, 112.5, 53.9, 30.3, 20.6; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{13}\text{BrN}_3$ 290.0287; Found 290.0288.

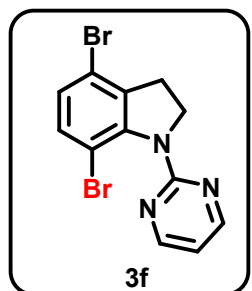
4-bromo-7-chloro-1-(pyrimidin-2-yl)indoline (2f): **2f** was prepared according to general



procedure (A) using indoline pyrimidine **1f** (70 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 20% EtOAc/Hexane afforded **2f** (50 mg, 64%) as a yellow solid. **R_f**: 0.31 (silica gel, 20% EtOAc/Hexane); **M. P.**: 93-98 °C; **IR (in CHCl₃, cm⁻¹):** ν_{max} ; 3018, 1575, 1556, 1449, 1433, 1409, 1214, 1137, 964; **¹H NMR (400 MHz, CDCl₃):** δ 8.49 (d, J = 4.8 Hz,

2H), 7.10 (s, 2H), 6.80 (t, J = 4.8 Hz, 1H), 4.43 (t, J = 8.0 Hz, 2H), 3.13 (t, J = 7.8 Hz, 2H); **¹³C NMR (100 MHz, CDCl₃):** δ 160.4, 157.5, 142.6, 137.1, 130.3, 127.1, 122.6, 117.1, 113.6, 52.9, 31.6; **HRMS (ESI) m/z:** [M + H]⁺ Calcd for C₁₂H₁₀BrClN₃ 309.9741; Found 309.9776.

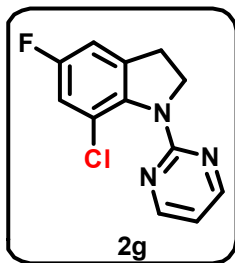
4,7-dibromo-1-(pyrimidin-2-yl)indoline (3f): **3f** was prepared according to general procedure (B) using indoline pyrimidine **1f** (53 mg, 0.25 mmol), halogenating source **F** (41 mg, 1.0 equiv).



The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **3f** (60 mg, 67%) as a white solid. **R_f**: 0.63 (silica gel, 20% EtOAc/Hexane); **M. P.**: 128-133 °C; **IR (in CHCl₃, cm⁻¹):** ν_{max} ; 3018, 1574, 1556, 1449, 1429, 1407, 1214, 1128, 1052, 993; **¹H NMR (400 MHz, CDCl₃):** δ 8.50 (d, J = 4.8 Hz, 2H), 7.27 (d, J = 8.5 Hz, 1H),

7.03 (d, J = 8.6 Hz, 1H), 6.81 (t, J = 4.8 Hz, 1H), 4.42 (t, J = 8.2 Hz, 2H), 3.14 (t, J = 8.2 Hz, 2H); **¹³C NMR (100 MHz, CDCl₃):** δ 160.3, 157.4, 144.4, 137.4, 133.3, 127.4, 118.0, 113.7, 111.3, 52.9, 31.7; **HRMS (ESI) m/z:** [M + H]⁺ Calcd for C₁₂H₁₀Br₂N₃ 353.9236; Found 353.9268.

7-chloro-5-fluoro-1-(pyrimidin-2-yl)indoline (2g): **2g** was prepared according to general

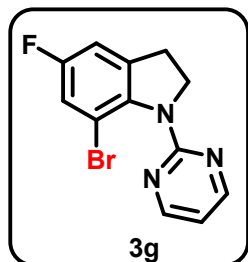


procedure (A) using indoline pyrimidine **1g** (54 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 20% EtOAc/Hexane afforded **2g** (35 mg, 55%) as a white solid. **R_f**: 0.35 (silica gel, 20% EtOAc/Hexane); **M. P.**: 118-123 °C; **IR (in CHCl₃, cm⁻¹):** ν_{max} ; 2989, 1578, 1556, 1470,

1451, 1413, 1281, 1192, 1096, 977, 766; **¹H NMR (400 MHz, CDCl₃):** δ 8.47 (d, J = 4.8 Hz, 2H), 6.98 (dd, J = 8.9 Hz, 2.5 Hz, 1H), 6.93–6.86 (m, 1H), 6.76 (t, J = 4.8 Hz, 1H), 4.44 (t, J = 7.8 Hz, 2H), 3.10 (t, J = 7.6 Hz, 2H); **¹³C NMR (100 MHz, CDCl₃):** δ 160.7, 159.1 (d, $J_{\text{C-F}}$ =

244.9 Hz), 157.4, 138.2, 124.2, 124.1, 115.5 (d, J_{C-F} = 26.3 Hz), 113.1, 110 (d, J_{C-F} = 23.7 Hz), 53.9, 30.4; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{12}H_{10}ClFN_3$ 250.0542; Found 250.0550.

7-bromo-5-fluoro-1-(pyrimidin-2-yl)indoline (3g): **3g** was prepared according to general procedure (B) using indoline pyrimidine **1g** (53 mg, 0.25 mmol), halogenating source **F** (41 mg,

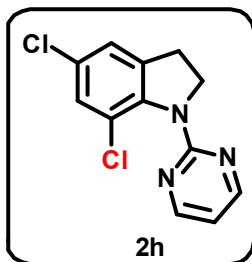


1.0 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **3g** (36 mg, 48%) as a yellow solid. R_f : 0.53 (silica gel, 20% EtOAc/Hexane); **M. P.:** 125-130 °C;

IR (in $CHCl_3$, cm^{-1}): ν_{max} ; 1512, 1434, 1384, 1209, 1140, 747, 711; **1H NMR (400 MHz, $CDCl_3$):** δ 8.48 (d, J = 4.8 Hz, 2H), 7.16 (dd, J = 8.7 Hz,

2.5 Hz, 1H), 6.97–6.91 (m, 1H), 6.77 (t, J = 4.8 Hz, 1H), 4.45 (t, J = 8.0 Hz, 2H), 3.11 (t, J = 7.6 Hz, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 160.7, 159.0 (d, J_{C-F} = 245.0 Hz), 157.4, 140.0, 138.4 (d, J_{C-F} = 9.0 Hz), 118.4 (d, J_{C-F} = 26.5 Hz), 113.3, 112.7, 112.6, 111.1 (d, J_{C-F} = 23.7 Hz), 54.0, 30.6; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{12}H_{10}BrFN_3$ 294.0037; Found 294.0035.

5,7-dichloro-1-(pyrimidin-2-yl)indoline (2h): **2h** was prepared according to general procedure

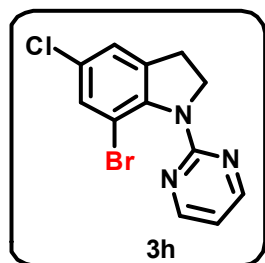


(A) using indoline pyrimidine **1h** (58 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **2h** (35 mg,

52%) as a yellow solid. R_f : 0.50 (silica gel, 20% EtOAc/Hexane); **M. P.:** 98-103 °C; **IR (in $CHCl_3$, cm^{-1}):** ν_{max} ; 3019, 1577, 1555, 1462, 1405,

1281, 1214, 1156, 823; **1H NMR (400 MHz, $CDCl_3$):** δ 8.48 (d, J = 4.8 Hz, 2H), 7.25–7.22 (m, 1H), 7.14–7.11 (m, 1H), 6.78 (t, J = 4.8 Hz, 1H), 4.43 (t, J = 7.9 Hz, 2H), 3.11 (t, J = 7.9 Hz, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 160.4, 157.5, 140.7, 138.2, 128.8, 128.5, 124.1, 123.2, 113.4, 53.7, 30.0; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{12}H_{10}Cl_2N_3$ 266.0246; Found 266.0243.

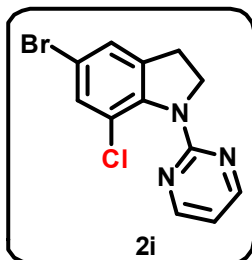
7-bromo-5-chloro-1-(pyrimidin-2-yl)indoline (3h): **3h** was prepared according to general procedure (B) using indoline pyrimidine **1h** (58 mg, 0.25 mmol), halogenating source **F** (41 mg,



1.0 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **3h** (29 mg, 37%) as a yellow solid. R_f : 0.45 (silica gel, 20% EtOAc/Hexane); **M. P.:** 128-133

°C; IR (in CHCl₃, cm⁻¹): ν_{\max} ; 3018, 1576, 1556, 1458, 1402, 1214, 1146, 860, 743; ¹H NMR (400 MHz, CDCl₃): δ 8.48 (d, J = 4.8 Hz, 2H), 7.41 (d, J = 1.9 Hz, 1H), 7.17 (d, J = 1.7 Hz, 1H), 6.79 (t, J = 4.8 Hz, 1H), 4.43 (t, J = 7.5 Hz, 2H), 3.11 (t, J = 7.5 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 160.4, 157.4, 142.5, 138.4, 131.3, 129.0, 123.8, 113.5, 112.8, 53.7, 30.2; HRMS (ESI) m/z : [M + H]⁺ Calcd for C₁₂H₁₀BrClN₃ 309.9741; Found 309.9747.

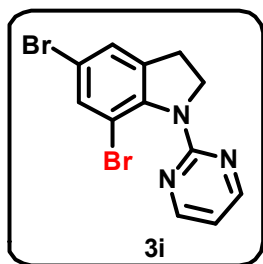
5-bromo-7-chloro-1-(pyrimidin-2-yl)indoline (2i): 2i was prepared according to general



procedure (A) using indoline pyrimidine 1i (70 mg, 0.25 mmol), halogenating source C (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 20% EtOAc/Hexane afforded 2i (38 mg, 49%) as a yellow solid. R_f : 0.37 (silica gel, 20% EtOAc/Hexane); M. P.: 112-117 °C; IR (in CHCl₃, cm⁻¹): ν_{\max} ; 3018,

2924, 1556, 1461, 1438, 1280, 1150, 1105, 1050, 916; ¹H NMR (400 MHz, CDCl₃): δ 8.48 (d, J = 4.8 Hz, 2H), 7.39–7.36 (m, 1H), 7.29–7.26 (m, 1H), 6.79 (t, J = 4.8 Hz, 1H), 4.42 (t, J = 8.0 Hz, 2H), 3.11 (t, J = 7.8 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 160.4, 157.5, 141.2, 138.6, 131.2, 126.1, 124.4, 115.9, 113.4, 53.7, 29.9; HRMS (ESI) m/z : [M + H]⁺ Calcd for C₁₂H₁₀BrClN₃ 309.9741; Found 309.9749.

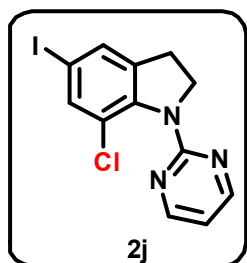
5,7-dibromo-1-(pyrimidin-2-yl)indoline (3i): 3i was prepared according to general procedure (B) using indoline pyrimidine 1i (70 mg, 0.25 mmol), halogenating source F (41 mg, 1.0 equiv).



The crude reaction mixture was purified by column chromatography using 13% EtOAc/Hexane afforded 3i (32 mg, 36%) as a yellow solid. R_f : 0.57 (silica gel, 20% EtOAc/Hexane); M. P.: 140-145 °C; IR (in CHCl₃, cm⁻¹): ν_{\max} ; 2926, 1576, 1556, 1457, 1436, 1399, 1214, 1140, 859; ¹H NMR (400 MHz, CDCl₃): δ 8.48 (d, J = 4.8 Hz, 2H), 7.55 (s, 1H), 7.30 (s, 1H),

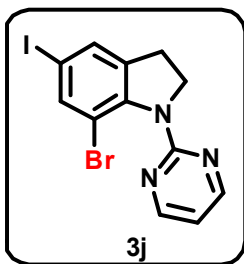
6.79 (t, J = 4.8 Hz, 1H), 4.43 (t, J = 8.0 Hz, 2H), 3.12 (t, J = 7.7 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 160.3, 157.4, 143.0, 138.8, 134.0, 126.6, 116.2, 113.5, 113.2, 53.8, 30.1; HRMS (ESI) m/z : [M + H]⁺ Calcd for C₁₂H₁₀Br₂N₃ 353.9236; Found 353.9238.

7-chloro-5-iodo-1-(pyrimidin-2-yl)indoline (2j): 2j was prepared according to general procedure (A) using indoline pyrimidine 1j (82 mg, 0.25 mmol), halogenating source C (41 mg, 1.2 equiv). The crude reaction mixture was



purified by column chromatography using 10% EtOAc/Hexane afforded **2j** (40 mg, 44%) as a white solid. R_f : 0.67 (silica gel, 20% EtOAc/Hexane); **M. P.**: 112-117 °C; **IR (in CHCl₃, cm⁻¹)**: ν_{max} ; 3016, 1576, 1556, 1460, 1437, 1397, 1281, 1214, 1049, 912, 742; **¹H NMR (400 MHz, CDCl₃)**: δ 8.48 (d, J = 4.8 Hz, 2H), 7.54 (s, 1H), 7.44 (s, 1H), 6.79 (t, J = 4.8 Hz, 1H), 4.40 (t, J = 7.8 Hz, 2H), 3.10 (t, J = 7.7 Hz, 2H); **¹³C NMR (100 MHz, CDCl₃)**: δ 160.3, 157.5, 141.9, 138.9, 136.9, 131.8, 124.6, 113.5, 85.9, 53.6, 29.6; **HRMS (ESI) m/z**: [M + H]⁺ Calcd for C₁₂H₁₀ClIN₃ 357.9602; Found 357.9600.

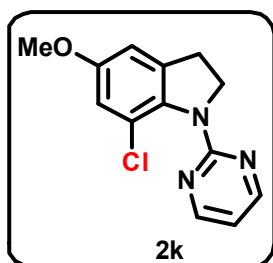
7-bromo-5-iodo-1-(pyrimidin-2-yl)indoline (3j): **3j** was prepared according to general



procedure (B) using indoline pyrimidine **1j** (82 mg, 0.25 mmol), halogenating source **F** (41 mg, 1.0 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **3j** (31 mg, 31%) as a white solid. R_f : 0.51 (silica gel, 20% EtOAc/Hexane); **M. P.**: 137-142 °C; **IR (in CHCl₃, cm⁻¹)**: ν_{max} ; 3019,

2922, 1573, 1556, 1456, 1432, 1396, 1214, 745; **¹H NMR (400 MHz, CDCl₃)**: δ 8.47 (d, J = 4.8 Hz, 2H), 7.72 (d, J = 1.5 Hz, 1H), 7.48 (d, J = 1.3 Hz, 1H), 6.79 (t, J = 4.8 Hz, 1H), 4.41 (t, J = 7.9 Hz, 2H), 3.11 (t, J = 7.8 Hz, 2H); **¹³C NMR (100 MHz, CDCl₃)**: δ 160.3, 157.4, 143.7, 139.6, 139.2, 132.4, 126.6, 113.6, 86.3, 53.7, 29.8; **HRMS (ESI) m/z**: [M + H]⁺ Calcd for C₁₂H₁₀BrIN₃ 401.9097; Found 401.9098.

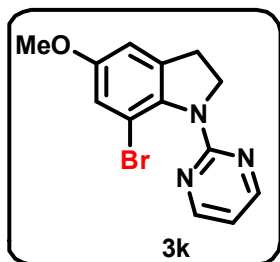
7-chloro-5-methoxy-1-(pyrimidin-2-yl)indoline (2k): **2k** was prepared according to general



procedure (A) using indoline pyrimidine **1k** (57 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **2k** (20 mg, 30%) as a colourless oil. R_f : 0.41 (silica gel, 20% EtOAc/Hexane); **IR (in CHCl₃, cm⁻¹)**: ν_{max} ; 3018, 1609, 1577, 1553,

1452, 1344, 1257, 1214, 1192, 1052, 877, 748; **¹H NMR (400 MHz, CDCl₃)**: δ 8.46 (d, J = 4.8 Hz, 2H), 6.78 (d, J = 2.3 Hz, 1H), 6.76-6.74 (m, 1H), 6.72 (t, J = 4.8 Hz, 1H), 4.42 (t, J = 7.7 Hz, 2H), 3.78 (s, 3H), 3.07 (t, J = 7.6 Hz, 2H); **¹³C NMR (100 MHz, CDCl₃)**: δ 161.0, 157.4, 156.9, 138.0, 135.3, 124.2, 113.2, 112.7, 110.2, 55.8, 53.8, 30.6; **HRMS (ESI) m/z**: [M + H]⁺ Calcd for C₁₃H₁₃ClN₃O 262.0742; Found 262.0746.

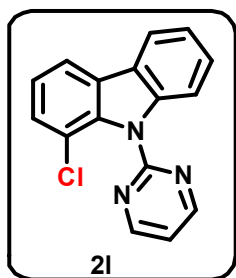
7-bromo-5-methoxy-1-(pyrimidin-2-yl)indoline (3k): **3k** was prepared according to general



procedure (B) using indoline pyrimidine **1k** (57 mg, 0.25 mmol), halogenating source **F** (41 mg, 1.0 equiv). The crude reaction mixture was purified by column chromatography using 10% EtOAc/Hexane afforded **3k** (26 mg, 34%) as a yellow solid. **R_f**: 0.61 (silica gel, 20% EtOAc/Hexane); **M. P.**: 115-120 °C; **IR (in CHCl₃, cm⁻¹):** ν_{\max} ; 2926,

1609, 1578, 1555, 1451, 1327, 1233, 1163, 1052, 991, 743; **¹H NMR (400 MHz, CDCl₃):** δ 8.46 (d, J = 4.8 Hz, 2H), 6.96 (s, 1H), 6.79 (s, 1H), 6.73 (t, J = 4.5 Hz, 1H), 4.42 (t, J = 7.5 Hz, 2H), 3.78 (s, 3H), 3.08 (t, J = 7.3 Hz, 2H); **¹³C NMR (100 MHz, CDCl₃):** δ 160.9, 157.4, 156.9, 138.2, 137.1, 116.1, 113.0, 112.8, 110.7, 55.8, 53.9, 30.8; **HRMS (ESI) m/z:** [M + H]⁺ Calcd for C₁₃H₁₃BrN₃O 306.0237; Found 306.0238.

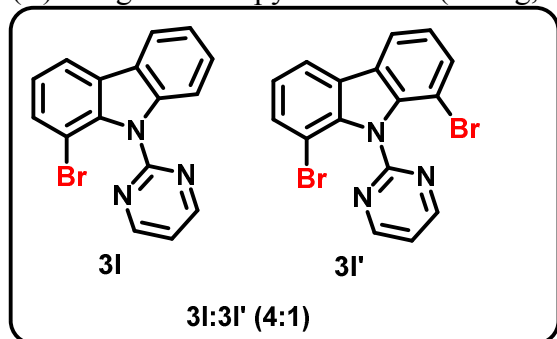
1-chloro-9-(pyrimidin-2-yl)-9H-carbazole (2l): **2l** was prepared according to general procedure



(A) using indoline pyrimidine **1l** (62 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 10% EtOAc/Hexane afforded **2l** (34 mg, 48%) as a colourless oil. **R_f**: 0.65 (silica gel, 20% EtOAc/Hexane); **IR (in CHCl₃, cm⁻¹):** ν_{\max} ; 3018, 1564, 1480, 1418, 1335, 1292, 1214, 1142, 1044, 925;

¹H NMR (400 MHz, CDCl₃): δ 8.90 (d, J = 4.8 Hz, 2H), 8.05 (d, J = 7.7 Hz, 1H), 8.00 (dd, J = 7.7 Hz, 1.0 Hz, 1H), 7.93 (d, J = 8.2 Hz, 1H), 7.48–7.41 (m, 2H), 7.35 (td, J = 7.2 Hz, 0.9 Hz, 1H), 7.31–7.26 (m, 2H); **¹³C NMR (100 MHz, CDCl₃):** δ 158.4, 157.8, 141.5, 136.5, 128.3, 128.0, 127.2, 124.5, 122.6, 122.2, 120.2, 119.2, 118.6, 118.5, 112.1; **HRMS (ESI) m/z:** [M + H]⁺ Calcd for C₁₆H₁₁ClN₃ 280.0636; Found 280.0634.

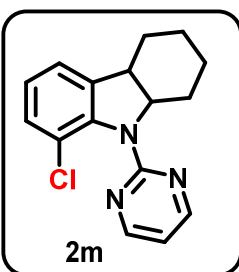
1-bromo-9-(pyrimidin-2-yl)-9H-carbazole (3l): **3l** was prepared according to general procedure (B) using indoline pyrimidine **1l** (62 mg, 0.25 mmol), halogenating source **F** (41 mg, 1.0 equiv).



The crude reaction mixture was purified by column chromatography using 10% EtOAc/Hexane afforded non separable mixture of **3l** and **3l'** (57 mg, 66%, 4:1) as a white solid. R_f : 0.50 (silica gel, 30% EtOAc/Hexane); **M. P.:** 122-127 °C; **IR (in CHCl₃, cm⁻¹):** ν_{max} ; 3019, 1565, 1418, 1214, 928, 742; **¹H NMR (400 MHz, CDCl₃):** δ 8.94 (d, J = 4.8 Hz, 0.4H), 8.92 (d, J = 4.8 Hz, 2H), 8.11–8.01 (m, 2.4 H), 7.88 (d, J = 8.3 Hz, 1H), 7.63 (dd, J = 7.8 Hz, 0.9 Hz, 1H), 7.57 (dd, J = 7.8 Hz, 0.9 Hz, 0.5 H), 7.55–7.50 (m, 0.27 H), 7.48–7.41 (m, 1H), 7.39–7.28 (m, 2H), 7.21 (t, J = 7.9 Hz, 1H), 7.16 (t, J = 7.9 Hz, 0.5H); **¹³C NMR (100 MHz, CDCl₃):** δ 158.5, 158.3, 157.7, 141.6, 138.1, 131.7, 131.2, 128.4, 127.1, 125.8, 124.4, 122.9, 122.2, 122.0, 121.5, 120.2, 119.5, 119.2, 118.7, 112.0, 106.9, 103.8; **HRMS (ESI) m/z:** [M + H]⁺ (**3l**) Calcd for C₁₆H₁₁BrN₃ 324.0131; Found 324.0129, **HRMS (ESI) m/z:** [M + H]⁺ (**3l'**) Calcd for C₁₆H₁₀Br₂N₃ 401.9236; Found 401.9236.

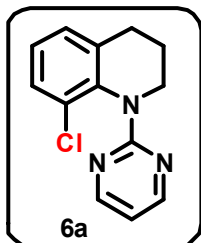
8-chloro-9-(pyrimidin-2-yl)-2,3,4,4a,9,9a-hexahydro-1H-carbazole (2m): **2m** was prepared according to general procedure (A) using indoline pyrimidine **1m** (63 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 10% EtOAc/Hexane afforded non separable mixture of **2m** (60 mg, 83%) as a colourless liquid. R_f : 0.50 (silica gel, 20% EtOAc/Hexane); **IR (in CHCl₃, cm⁻¹):** ν_{max} ; 3035, 2527, 1710, 1505, 1315, 1027, 970; **¹H NMR (400 MHz, CDCl₃):** δ 8.45 (d, J = 4.8 Hz, 2H), 7.23 (dt, J = 7.8 Hz, 1.2 Hz, 1H), 7.10–7.00 (m, 2H), 6.71 (t, J = 4.8 Hz, 1H), 4.88–4.78 (m, 1H), 3.68 (t, J = 6.2 Hz, 1H), 2.33–2.19 (m, 2H), 1.90–1.74 (m, 1H), 1.69–1.61 (m, 1H), 1.57–1.50 (m, 1H), 1.43–1.28 (m, 2H), 1.22–1.09 (m, 1H); **¹³C NMR (100 MHz, CDCl₃):** δ 160.2, 157.6, 141.3, 139.7, 128.7, 124.8, 121.0, 112.8, 66.6, 41.6, 28.4, 24.7, 23.0, 20.9; **HRMS (ESI) m/z:** [M + H]⁺ Calcd for C₁₆H₁₇ClN₃ 286.1106; Found 286.1101.

8-chloro-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (6a): **6a** was prepared according to general procedure (A) using tetrahydroquinoline pyrimidine **5a** (53 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture



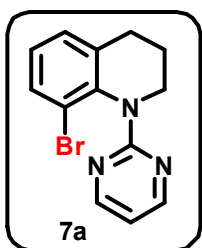
halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 10% EtOAc/Hexane afforded non separable mixture of **2m** (60 mg, 83%) as a colourless liquid. R_f : 0.50 (silica gel, 20% EtOAc/Hexane); **IR (in CHCl₃, cm⁻¹):** ν_{max} ; 3035, 2527, 1710, 1505, 1315, 1027, 970; **¹H NMR (400 MHz, CDCl₃):** δ 8.45 (d, J = 4.8 Hz, 2H), 7.23 (dt, J = 7.8 Hz, 1.2 Hz, 1H), 7.10–7.00 (m, 2H), 6.71 (t, J = 4.8 Hz, 1H), 4.88–4.78 (m, 1H), 3.68 (t, J = 6.2 Hz, 1H), 2.33–2.19 (m, 2H), 1.90–1.74 (m, 1H), 1.69–1.61 (m, 1H), 1.57–1.50 (m, 1H), 1.43–1.28 (m, 2H), 1.22–1.09 (m, 1H); **¹³C NMR (100 MHz, CDCl₃):** δ 160.2, 157.6, 141.3, 139.7, 128.7, 124.8, 121.0, 112.8, 66.6, 41.6, 28.4, 24.7, 23.0, 20.9; **HRMS (ESI) m/z:** [M + H]⁺ Calcd for C₁₆H₁₇ClN₃ 286.1106; Found 286.1101.

8-chloro-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (6a): **6a** was prepared according to general procedure (A) using tetrahydroquinoline pyrimidine **5a** (53 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture



was purified by column chromatography using 12% EtOAc/Hexane afforded **6a** (59 mg, 95%) as a colourless oil. **R_f**: 0.53 (silica gel, 20% EtOAc/Hexane); **M. P.**: 78-83 °C; **IR (in CHCl₃, cm⁻¹)**: ν_{\max} ; 2929, 1578, 1555, 1463, 1356, 1287, 1214, 1117, 1061, 826, 743; **¹H NMR (400 MHz, CDCl₃)**: δ 8.41 (d, J = 4.7 Hz, 2H), 7.27 (dd, J = 7.6 Hz, 1.6 Hz, 1H), 7.13–7.01 (m, 2H), 6.67 (t, J = 4.7 Hz, 1H), 4.06 (s, 2H), 2.76 (t, J = 6.8 Hz, 2H), 2.11–1.92 (m, 2H); **¹³C NMR (100 MHz, CDCl₃)**: δ 161.3, 157.6, 138.3, 135.9, 130.6, 127.7, 126.8, 125.3, 112.2, 45.6, 27.0, 24.3; **HRMS (ESI) m/z**: [M + H]⁺ Calcd for C₁₃H₁₃ClN₃ 246.0793; Found 246.0789.

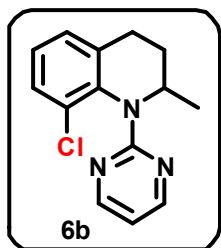
8-bromo-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (7a): **7a** was prepared according to



general procedure (B) using tetrahydroquinoline pyrimidine **5a** (62 mg, 0.25 mmol), halogenating source **F** (41 mg, 1.0 equiv). The crude reaction mixture was purified by column chromatography using 10% EtOAc/Hexane afforded **7a** (57 mg, 78%) as a white solid. **R_f**: 0.49 (silica gel, 20% EtOAc/Hexane); **M. P.**: 98-103 °C; **IR (in CHCl₃, cm⁻¹)**: ν_{\max} ; 2953, 1578, 1556, 1461, 1430,

1355, 1198, 1117, 1059, 992; **¹H NMR (400 MHz, CDCl₃)**: δ 8.41 (d, J = 4.8 Hz, 2H), 7.46 (d, J = 7.8 Hz, 1H), 7.14 (d, J = 7.0 Hz, 1H), 6.99 (t, J = 7.6 Hz, 1H), 6.66 (t, J = 4.8 Hz, 1H), 4.06 (s, 2H), 2.75 (t, J = 6.8 Hz, 2H), 2.07–1.95 (m, 2H); **¹³C NMR (100 MHz, CDCl₃)**: δ 161.3, 157.7, 139.9, 136.5, 130.9, 127.5, 125.9, 121.2, 112.2, 45.5, 27.0, 24.3; **HRMS (ESI) m/z**: [M + H]⁺ Calcd for C₁₃H₁₃BrN₃ 290.0287; Found 290.0284.

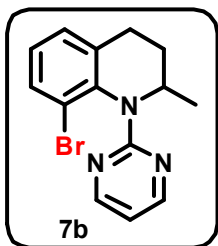
8-chloro-2-methyl-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (6b): **6b** was prepared



according to general procedure (A) using tetrahydroquinoline pyrimidine **5b** (57 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 10% EtOAc/Hexane afforded **6b** (57 mg, 86%) as a white solid. **R_f**: 0.70 (silica gel, 20% EtOAc/Hexane); **M. P.**: 122-127 °C; **IR (in CHCl₃, cm⁻¹)**: ν_{\max} ;

3018, 1582, 1553, 1470, 1457, 1301, 1214, 1128, 1050, 743; **¹H NMR (400 MHz, CDCl₃)**: δ 8.38 (s, 2H), 7.32–7.27 (m, 1H), 7.14–7.04 (m, 2H), 6.63 (t, J = 4.7 Hz, 1H), 5.04–4.91 (m, 1H), 2.66–2.52 (m, 2H), 2.52–2.39 (m, 1H), 1.49–1.36 (m, 1H), 1.26 (d, J = 6.8 Hz, 3H); **¹³C NMR (100 MHz, CDCl₃)**: δ 160.7, 157.6, 138.7, 136.3, 131.7, 127.8, 125.7, 125.6, 111.8, 51.2, 33.8, 26.8, 20.8; **HRMS (ESI) m/z**: [M + H]⁺ Calcd for C₁₄H₁₅ClN₃ 260.0949; Found 260.0947.

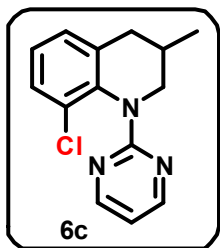
8-bromo-2-methyl-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (7b): **7b** was prepared



according to general procedure (B) using tetrahydroquinoline pyrimidine **5b** (57 mg, 0.25 mmol), halogenating source **F** (41 mg, 1.0 equiv). The crude reaction mixture was purified by column chromatography using 10% EtOAc/Hexane afforded **7b** (48 mg, 63%) as a white solid. **R_f**: 0.67 (silica gel, 20% EtOAc/Hexane); **M. P.**: 133-138 °C; **IR (in CHCl₃, cm⁻¹):** ν_{\max} ;

3018, 1579, 1554, 1467, 1431, 1214, 1139, 1050, 929; **¹H NMR (400 MHz, CDCl₃):** δ 8.38 (s, 2H), 7.48 (d, $J = 7.5$ Hz, 1H), 7.15 (d, $J = 7.5$ Hz, 1H), 7.01 (t, $J = 7.7$ Hz, 1H), 6.63 (t, $J = 4.7$ Hz, 1H), 5.04–4.94 (m, 1H), 2.65–2.51 (m, 2H), 2.49–2.42 (m, 1H), 1.45–1.36 (m, 1H), 1.26 (d, $J = 6.4$ Hz, 3H); **¹³C NMR (100 MHz, CDCl₃):** δ 160.7, 157.7, 139.3, 137.9, 131.0, 126.3, 126.2, 122.3, 111.8, 51.3, 34.0, 27.1, 20.9; **HRMS (ESI) m/z:** [M + H]⁺ Calcd for C₁₄H₁₅BrN₃ 304.0444; Found 304.0442.

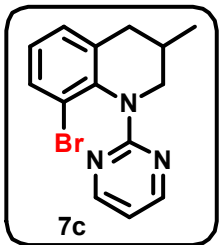
8-chloro-3-methyl-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (6c): **6c** was prepared



according to general procedure (A) using tetrahydroquinoline pyrimidine **5c** (57 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **6c** (49 mg, 75%) as a colourless oil. **R_f**: 0.49 (silica gel, 20% EtOAc/Hexane); **IR (in CHCl₃, cm⁻¹):** ν_{\max} ;

3018, 2927, 1579, 1555, 1463, 1421, 1214, 1058, 742; **¹H NMR (400 MHz, CDCl₃):** δ 8.41 (d, $J = 4.8$ Hz, 2H), 7.26 (dd, $J = 7.5$ Hz, 1.7 Hz, 1H), 7.10–7.01 (m, 2H), 6.67 (t, $J = 4.8$ Hz, 1H), 4.42 (dd, $J = 12.3$ Hz, 4.8 Hz, 1H), 3.37 (t, $J = 11.5$ Hz, 1H), 2.89 (dd, $J = 15.8$ Hz, 5.7 Hz, 1H), 2.41 (dd, $J = 15.6$ Hz, 9.8 Hz, 1H), 2.19–2.04 (m, 1H) 1.07 (d, $J = 6.6$ Hz, 3H); **¹³C NMR (100 MHz, CDCl₃):** δ 161.5, 157.6, 137.8, 135.2, 130.4, 127.6, 127.0, 125.2, 112.3, 52.8, 35.8, 30.8, 19.5; **HRMS (ESI) m/z:** [M + H]⁺ Calcd for C₁₄H₁₅ClN₃ 260.0949; Found 260.0944.

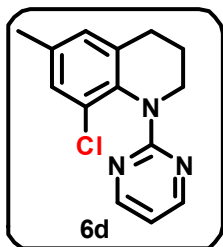
8-bromo-3-methyl-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (7c): **7c** was prepared



according to general procedure (B) using tetrahydroquinoline pyrimidine **5c** (57 mg, 0.25 mmol), halogenating source **F** (41 mg, 1.0 equiv). The crude reaction mixture was purified by column chromatography using 10% EtOAc/Hexane afforded **7c** (57 mg, 74%) as a colourless oil. **R_f**: 0.61 (silica gel, 20% EtOAc/Hexane); **IR (in CHCl₃, cm⁻¹):** ν_{\max} ; 2927, 1578, 1555,

1460, 1419, 1214, 1152, 1057, 989; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 8.41 (d, $J = 4.8$ Hz, 2H), 7.45 (dt, $J = 7.9$ Hz, 0.5 Hz, 1H), 7.11 (dt, $J = 7.5$ Hz, 0.6 Hz, 1H), 6.97 (t, $J = 7.6$ Hz, 1H), 6.67 (t, $J = 4.8$ Hz, 1H), 4.50–4.31 (m, 1H), 3.47–3.35 (m, 1H), 2.89 (dd, $J = 15.8$ Hz, 5.8 Hz, 1H), 2.41 (dd, $J = 15.8$ Hz, 9.7 Hz, 1H), 2.21–2.06 (m, 1H) 1.07 (d, $J = 6.6$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 161.5, 157.7, 139.4, 135.7, 130.9, 127.7, 125.7, 121.0, 112.3, 52.8, 35.9, 30.9, 19.6; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{14}\text{H}_{15}\text{BrN}_3$ 304.0444; Found 304.0440.

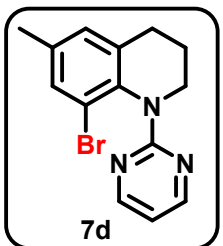
8-chloro-6-methyl-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (6d): **6d** was prepared



according to general procedure (A) using tetrahydroquinoline pyrimidine **5d** (57 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 10% EtOAc/Hexane afforded **6d** (37 mg, 56%) as a colourless oil. R_f : 0.70 (silica gel, 20% EtOAc/Hexane); IR (in CHCl_3 , cm^{-1}): ν_{max} ; 3018, 1581, 1555,

1449, 1433, 1214, 742; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 8.40 (d, $J = 4.8$ Hz, 2H), 7.10 (d, $J = 1.0$ Hz, 1H), 6.90 (d, $J = 0.7$ Hz, 1H), 6.64 (t, $J = 4.8$ Hz, 1H), 4.04 (s, 2H), 2.72 (t, $J = 7.0$ Hz, 2H), 2.29 (s, 3H), 2.05–1.92 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 161.4, 157.6, 135.6, 135.5, 135.3, 130.1, 128.2, 127.6, 112.0, 45.6, 26.9, 24.2, 20.7; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{14}\text{H}_{15}\text{ClN}_3$ 260.0949; Found 260.0944.

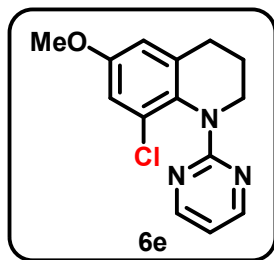
8-bromo-6-methyl-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (7d): **7d** was prepared



according to general procedure (B) using tetrahydroquinoline pyrimidine **5d** (57 mg, 0.25 mmol), halogenating source **F** (41 mg, 1.0 equiv). The crude reaction mixture was purified by column chromatography using 10% EtOAc/Hexane afforded **7d** (58 mg, 75%) as a colourless oil. R_f : 0.69 (silica gel, 20% EtOAc/Hexane); IR (in CHCl_3 , cm^{-1}): ν_{max} ; 2926, 1580, 1554,

1433, 1301, 1216, 1195, 991, 743; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 8.40 (d, $J = 4.8$ Hz, 2H), 7.29 (d, $J = 1.0$ Hz, 1H), 6.95 (d, $J = 0.8$ Hz, 1H), 6.64 (t, $J = 4.8$ Hz, 1H), 4.41–3.65 (m, 2H), 2.71 (t, $J = 7.0$ Hz, 2H), 2.29 (s, 3H), 2.03–1.92 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 161.4, 157.7, 137.2, 136.0, 135.8, 131.3, 128.3, 120.8, 112.0, 45.4, 26.9, 24.3, 20.6; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{14}\text{H}_{15}\text{BrN}_3$ 304.0444; Found 304.0447.

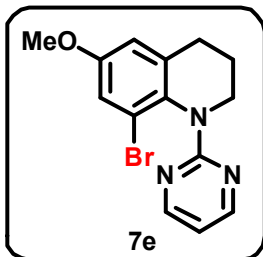
8-chloro-6-methoxy-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (6e): 6e was prepared according to general procedure (A) using tetrahydroquinoline pyrimidine 5e (61 mg, 0.25 mmol),



halogenating source C (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded 6e (55 mg, 79%) as a white solid. R_f : 0.45 (silica gel, 20% EtOAc/Hexane); **M. P.:** 118-123 °C; **IR (in CHCl₃, cm⁻¹):** ν_{max} ; 3033, 2892, 1572, 1551, 1452, 1416, 1320, 1241, 1121, 1047, 990, 798; **¹H**

NMR (400 MHz, CDCl₃): δ 8.40 (d, J = 4.7 Hz, 2H), 6.86 (d, J = 2.7 Hz, 1H), 6.66 (d, J = 2.8 Hz, 1H), 6.63 (t, J = 4.7 Hz, 1H), 4.50–3.85 (m, 2H), 3.78 (s, 3H), 2.72 (t, J = 6.8 Hz, 2H), 2.05–1.92 (m, 2H); **¹³C NMR (100 MHz, CDCl₃):** δ 161.4, 157.6, 156.7, 136.7, 131.4, 131.1, 113.2, 112.5, 111.8, 55.5, 45.3, 27.2, 24.1; **HRMS (ESI) m/z:** [M + H]⁺ Calcd for C₁₄H₁₅ClN₃O 276.0898; Found 276.0895.

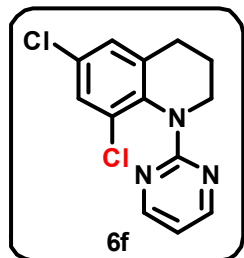
8-bromo-6-methoxy-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (7e): 7e was prepared according to general procedure (B) using tetrahydroquinoline pyrimidine 5e (61 mg, 0.25 mmol),



halogenating source F (41 mg, 1.0 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded 7e (58 mg, 78%) as a white solid. R_f : 0.43 (silica gel, 20% EtOAc/Hexane); **M. P.:** 132-137 °C; **IR (in CHCl₃, cm⁻¹):** ν_{max} ; 2926, 1582, 1554, 1436, 1414, 1270, 1125, 991, 766; **¹H NMR (400 MHz,**

CDCl₃): δ 8.40 (d, J = 4.6 Hz, 2H), 7.05 (d, J = 2.7 Hz, 1H), 6.71 (d, J = 2.7 Hz, 1H), 6.63 (t, J = 4.7 Hz, 1H), 4.59–3.12 (s, 2H), 3.78 (s, 3H), 2.71 (t, J = 6.6 Hz, 2H), 2.09–1.89 (m, 2H); **¹³C NMR (100 MHz, CDCl₃):** δ 161.5, 157.7, 156.9, 137.2, 133.1, 121.5, 116.2, 113.2, 111.8, 55.5, 45.2, 27.3, 24.1; **HRMS (ESI) m/z:** [M + H]⁺ Calcd for C₁₄H₁₅BrN₃O 320.0393; Found 320.0390.

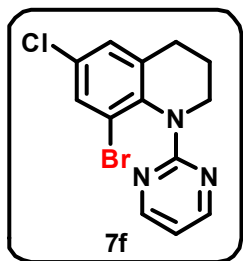
6,8-dichloro-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (6f): 6f was prepared according



to general procedure (A) using tetrahydroquinoline pyrimidine 5f (62 mg, 0.25 mmol), halogenating source C (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded 6f (52 mg, 73%) as a white solid. R_f : 0.57 (silica gel, 20% EtOAc/Hexane); **M. P.:** 85-90 °C; **IR (in CHCl₃, cm⁻¹):** ν_{max} ; 3019, 1579,

1556, 1462, 1432, 1407, 1214, 1117, 928; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 8.41 (d, $J = 4.8$ Hz, 2H), 7.28 (d, $J = 2.3$ Hz, 1H), 7.09 (d, $J = 2.3$ Hz, 1H), 6.69 (t, $J = 4.8$ Hz, 1H), 4.05 (s, 2H), 2.74 (t, $J = 6.9$ Hz, 2H), 2.04–1.94 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 161.1, 157.7, 137.1, 136.9, 131.3, 129.9, 127.5, 126.9, 112.5, 45.6, 27.0, 24.0; **HRMS (ESI)** m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{12}\text{Cl}_2\text{N}_3$ 280.0403; Found 280.0397.

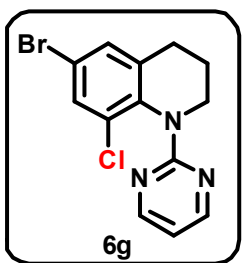
8-bromo-6-chloro-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (7f): **7f** was prepared according to general procedure (B) using tetrahydroquinoline pyrimidine **5f** (62 mg, 0.25 mmol),



halogenating source **F** (41 mg, 1.0 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **7f** (65 mg, 80%) as a white solid. **R_f**: 0.55 (silica gel, 20% EtOAc/Hexane); **M. P.**: 100–105 °C; **IR** (in CHCl_3 , cm^{-1}): ν_{max} ; 3018, 1579, 1556, 1460, 1431, 1404, 1214, 860; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 8.42 (d, $J = 4.7$ Hz, 2H),

7.46 (d, $J = 2.3$ Hz, 1H), 7.17–7.12 (m, 1H), 6.69 (t, $J = 4.7$ Hz, 1H), 4.05 (s, 2H), 2.74 (t, $J = 6.7$ Hz, 2H), 2.04–1.93 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 161.1, 157.7, 138.7, 137.3, 130.5, 130.3, 127.6, 121.6, 112.5, 48.5, 27.0, 24.0; **HRMS (ESI)** m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{12}\text{BrClN}_3$ 323.9898; Found 323.9896.

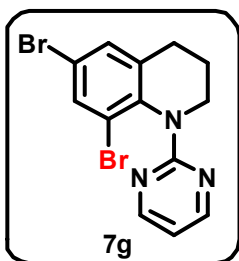
6-bromo-8-chloro-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (6g): **6g** was prepared according to general procedure (A) using tetrahydroquinoline pyrimidine **5g** (73 mg, 0.25



mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 10% EtOAc/Hexane afforded **6g** (52 mg, 64%) as a white solid. **R_f**: 0.60 (silica gel, 20% EtOAc/Hexane); **M. P.**: 125–130 °C; **IR** (in CHCl_3 , cm^{-1}): ν_{max} ; 3019, 1578, 1556, 1460, 1431, 1402, 1214, 857; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 8.41 (d,

$J = 4.7$ Hz, 2H), 7.42 (d, $J = 2.0$ Hz, 1H), 7.24 (d, $J = 2.0$ Hz, 1H), 6.70 (t, $J = 4.7$ Hz, 1H), 4.05 (s, 2H), 2.75 (t, $J = 6.7$ Hz, 2H), 2.03–1.93 (m, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 161.1, 157.7, 137.6, 137.3, 131.5, 130.3, 129.8, 117.5, 112.6, 45.6, 26.9, 24.0; **HRMS (ESI)** m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{12}\text{BrClN}_3$ 323.9898, found 323.9896.

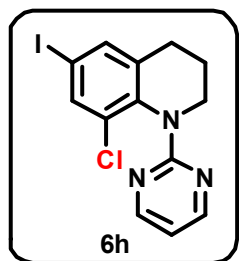
6,8-dibromo-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (7g): **7g** was prepared according



to general procedure (B) using tetrahydroquinoline pyrimidine **5g** (73 mg, 0.25 mmol), halogenating source **F** (41 mg, 1.0 equiv). The crude reaction mixture was purified by column chromatography using 10% EtOAc/Hexane afforded **7g** (64 mg, 69%) as a white solid. *R_f*: 0.60 (silica gel, 20% EtOAc/Hexane); **M. P.:** 125-130 °C; **IR (in CHCl₃, cm⁻¹):** *v*_{max};

3018, 1577, 1556, 1458, 1299, 1214, 1118, 1025, 928, 742; **¹H NMR (400 MHz, CDCl₃):** δ 8.41 (d, *J* = 4.7 Hz, 2H), 7.61 (d, *J* = 2.0 Hz, 1H), 7.28 (d, *J* = 2.0 Hz, 1H), 6.69 (t, *J* = 4.7 Hz, 1H), 4.04 (s, 2H), 2.74 (t, *J* = 6.7 Hz, 2H), 2.04–1.93 (m, 2H); **¹³C NMR (100 MHz, CDCl₃):** δ 161.1, 157.7, 137.6, 137.3, 131.5, 130.3, 129.8, 117.5, 112.6, 45.6, 26.9, 24.0; **HRMS (ESI) m/z:** [M + H]⁺ Calcd for C₁₃H₁₂Br₂N₃ 367.9392; Found 367.9391.

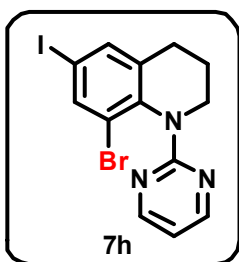
8-chloro-6-iodo-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (6h): **6h** was prepared according to general procedure (A) using tetrahydroquinoline pyrimidine **5h** (85 mg, 0.25



mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **6h** (72 mg, 77%) as a white solid. *R_f*: 0.45 (silica gel, 20% EtOAc/Hexane); **M. P.:** 150-155 °C; **IR (in CHCl₃, cm⁻¹):** *v*_{max}; 2982, 1592, 1491, 1383, 1306, 1214, 1062, 996, 741; 2947, 1582, 1555, 1458, 1397,

1214, 1088, 992, 749; **¹H NMR (400 MHz, CDCl₃):** δ 8.42 (d, *J* = 4.7 Hz, 2H), 7.78 (d, *J* = 1.8 Hz, 1H), 7.50–7.44 (m, 1H), 6.70 (t, *J* = 4.8 Hz, 1H), 4.04 (s, 2H), 2.71 (t, *J* = 7.0 Hz, 2H), 2.02–1.94 (m, 2H); **¹³C NMR (100 MHz, CDCl₃):** δ 161.1, 157.7, 139.9, 138.8, 138.2, 136.4, 122.0, 112.6, 88.8, 45.5, 26.8, 24.0; **HRMS (ESI) m/z:** [M + H]⁺ Calcd for C₁₃H₁₂ClIN₃ 371.9759; Found 371.9755.

8-bromo-6-iodo-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline (7h): **7h** was prepared

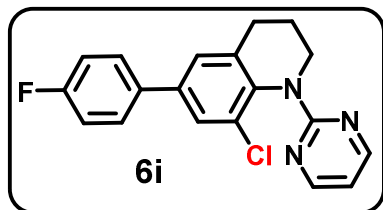


according to general procedure (B) using tetrahydroquinoline pyrimidine **5h** (85 mg, 0.25 mmol), halogenating source **F** (41 mg, 1.0 equiv). The crude reaction mixture was purified by column chromatography using 15% EtOAc/Hexane afforded **7h** (61 mg, 58%) as a white solid. *R_f*: 0.49 (silica gel, 20% EtOAc/Hexane); **M. P.:** 170-175 °C; **IR (in CHCl₃, cm⁻¹):** *v*_{max};

2928, 1583, 1556, 1426, 1354, 1229, 1154, 1119, 1024, 992; **¹H NMR (400 MHz, CDCl₃):** δ

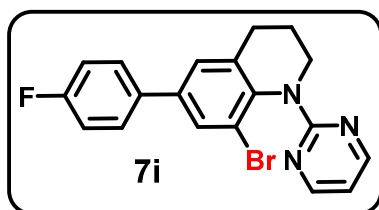
8.41 (d, $J = 4.7$ Hz, 2H), 7.59 (d, $J = 1.9$ Hz, 1H), 7.43 (d, $J = 1.9$ Hz, 1H), 6.70 (t, $J = 4.7$ Hz, 1H), 4.04 (s, 2H), 2.73 (t, $J = 6.7$ Hz, 2H), 2.05–1.92 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 161.0, 157.7, 138.3, 137.6, 135.9, 135.7, 131.5, 112.6, 88.1, 45.6, 26.7, 24.0; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{12}\text{BrIN}_3$ 415.9254; Found 415.9252.

8-chloro-6-(4-fluorophenyl)-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline: **6i** was prepared according to general procedure (A) using tetrahydroquinoline pyrimidine **1i** (76 mg, 0.25 mmol),



halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 7% EtOAc/Hexane afforded **6i** (42 mg, 49%) as a white solid. R_f : 0.50 (silica gel, 10% EtOAc/Hexane); **M. P.**: 128–133 °C; **IR** (in CHCl_3 , cm^{-1}): ν_{max} : 2360, 2340, 1576, 1557, 1521, 1464, 1435, 1418, 1234, 1197, 1159, 911; ^1H NMR (400 MHz, CDCl_3): δ 8.44 (d, $J = 4.7$ Hz, 2H), 7.56–7.48 (m, 2H), 7.46 (d, $J = 1.9$ Hz, 1H), 7.28–7.26 (m, 1H), 7.11 (t, $J = 8.6$ Hz, 2H), 6.70 (t, $J = 4.8$ Hz, 1H), 4.10 (bs, 2H), 2.83 (t, $J = 6.7$ Hz, 2H), 2.16 (q, $J = 6.6$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 162.4 (d, $J = 247$ Hz), 161.3, 157.7, 137.4, 137.3, 136.0, 135.9 (d, $J = 3.2$ Hz), 130.8, 128.5 (d, $J = 8.0$ Hz), 126.3, 125.4, 115.6 (d, $J = 21.6$ Hz), 112.3, 45.8, 27.3, 24.3; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{16}\text{ClFN}_3$ 340.1011; Found 340.1014.

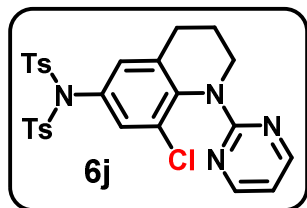
8-bromo-6-(4-fluorophenyl)-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline: **7i** was prepared according to general procedure (B) using tetrahydroquinoline pyrimidine **1i** (76 mg, 0.25 mmol),



halogenating source **F** (41 mg, 1.0 equiv). The crude reaction mixture was purified by column chromatography using 10% EtOAc/Hexane afforded **7i** (58 mg, 61%) as a white solid. R_f : 0.50 (silica gel, 20% EtOAc/Hexane); **M. P.**: 147–152 °C; **IR** (in CHCl_3 , cm^{-1}): ν_{max} : 2360, 1576, 1579, 1556, 1515, 1464, 1434, 1417, 1230, 1197, 1159, 908; ^1H NMR (400 MHz, CDCl_3): δ 8.44 (d, $J = 4.7$ Hz, 2H), 7.65 (d, $J = 2.0$ Hz, 1H), 7.57–7.47 (m, 2H), 7.35–7.258 (m, 1H), 7.16–7.06 (m, 2H), 6.69 (t, $J = 4.8$ Hz, 1H), 4.09 (bs, 2H), 2.82 (t, $J = 6.9$ Hz, 2H), 2.04 (q, $J = 6.6$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 162.4 (d, $J = 247$ Hz), 161.3, 157.7, 139.0, 137.9, 136.5, 135.8 (d, $J = 2.8$ Hz), 129.5, 128.5 (d, $J = 7.9$ Hz), 126.1, 115.6 (d, $J = 21.6$ Hz), 112.4, 45.7, 27.3, 24.3; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{16}\text{BrFN}_3$ 384.0506; Found 384.0511.

N-(8-chloro-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinolin-6-yl)-4-methyl-N-

tosylbenzenesulfonamide: 6j was prepared according to general procedure (A) using tetrahydroquinoline pyrimidine **1j** (133 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2

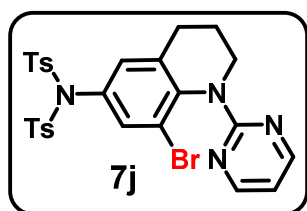


equiv). The crude reaction mixture was purified by column chromatography using 30% EtOAc/Hexane afforded **6j** (50 mg, 35%) as a white solid. **R_f**: 0.50 (silica gel, 50% EtOAc/Hexane); **M. P.**: 195-200 °C; **IR (in CHCl₃, cm⁻¹)**: *v*_{max}; 2925, 1716, 1698, 1577, 1557,

1521, 1507, 1457, 1417, 1379, 1228, 1169, 1087, 930; **¹H NMR (400 MHz, CDCl₃)**: δ 8.42 (d, *J* = 4.8 Hz, 2H), 7.85 (d, *J* = 8.4 Hz, 4H), 7.35 (d, *J* = 8.1 Hz, 4H), 6.91 (d, *J* = 2.3 Hz, 1H), 6.76 (d, *J* = 2.3 Hz, 1H), 6.73 (t, *J* = 4.8 Hz, 1H), 4.06 (t, *J* = 6.5 Hz, 2H), 2.70 (t, *J* = 6.8 Hz, 2H), 2.47 (s, 6H), 1.98 (q, *J* = 6.5 Hz, 2H); **¹³C NMR (100 MHz, CDCl₃)**: δ 161.0, 157.6, 145.1, 140.3, 136.5, 135.6, 130.7, 130.5, 130.1, 129.9, 129.5, 128.6, 112.9, 45.8, 27.0, 23.9, 21.7; **HRMS (ESI) m/z**: [M+H]⁺ calcd for C₂₇H₂₆ClN₄O₄S₂ 569.1079; Found 569.1072.

N-(8-bromo-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinolin-6-yl)-4-methyl-N-

tosylbenzenesulfonamide: 7j was prepared according to general procedure (B) using



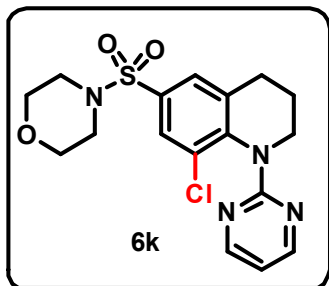
tetrahydroquinoline pyrimidine **1j** (133 mg, 0.25 mmol), halogenating source **F** (41 mg, 1.0 equiv). The crude reaction mixture was purified by column chromatography using 30% EtOAc/Hexane afforded **7j** (76 mg, 49%) as a white solid. **R_f**: 0.50 (silica gel, 50% EtOAc/Hexane);

M. P.: 168-173 °C; **IR (in CHCl₃, cm⁻¹)**: *v*_{max}; 3042, 1578, 1556, 1431, 1409, 1379, 1188, 1169, 903; **¹H NMR (400 MHz, CDCl₃)**: δ 8.42 (d, *J* = 4.7 Hz, 2H), 7.85 (d, *J* = 8.2 Hz, 4H), 7.35 (d, *J* = 8.1 Hz, 4H), 7.07 (d, *J* = 2.3 Hz, 1H), 6.82 (d, *J* = 2.3 Hz, 1H), 6.73 (t, *J* = 4.7 Hz, 1H), 4.12-4.03 (m, 2H), 2.70 (t, *J* = 6.7 Hz, 2H), 2.47 (s, 6H), 1.98 (q, *J* = 6.6 Hz, 2H); **¹³C NMR (100 MHz, CDCl₃)**: δ 161.0, 157.6, 145.1, 142.0, 136.5, 136.0, 133.7, 130.5, 130.4, 129.5, 129.4, 128.7, 112.9, 45.7, 27.0, 23.9, 21.7; **HRMS (ESI) m/z**: [M+H]⁺ calcd for C₂₇H₂₆BrN₄O₄S₂ 613.0573; Found 613.0561.

4-((8-chloro-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinolin-6-yl)sulfonyl)morpholine: 6k

was prepared according to general procedure (A) using tetrahydroquinoline pyrimidine **1k** (91 mg, 0.25 mmol), halogenating source **C** (41 mg, 1.2 equiv). The crude reaction mixture was purified by column chromatography using 50% EtOAc/Hexane afforded **6k** (39 mg, 39%) as a

white solid. Rf: 0.48 (silica gel, 60% EtOAc/Hexane); **M. P.:** 180-185 °C; **IR (in CHCl₃, cm⁻¹):**

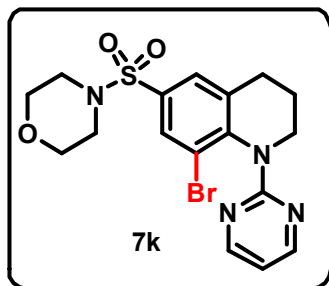


ν_{max} : 2863, 1731, 1555, 1261, 1014, 800, 661; **¹H NMR (400 MHz, CDCl₃):** δ 8.45 (d, J = 4.8 Hz, 2H), 7.64 (d, J = 2.0 Hz, 1H), 7.47 (d, J = 2.0 Hz, 1H), 6.79 (t, J = 4.7 Hz, 1H), 4.09 (t, J = 6.4 Hz, 2H), 3.81–3.75 (m, 4H), 3.11–3.05 (m, 4H), 2.86 (t, J = 6.6 Hz, 2H), 2.08–2.01 (m, 2H); **¹³C NMR (100 MHz, CDCl₃):** δ 160.9, 157.7, 142.9, 136.1, 131.2, 130.8, 127.3, 126.2, 113.4, 66.1, 46.2, 45.9, 27.4,

23.9; **HRMS (ESI) m/z:** [M+H]⁺ calcd for C₁₇H₂₀ClN₄O₃S 395.0939; Found 395.0934.

4-((8-bromo-1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinolin-6-yl)sulfonyl)morpholine: **7k**

was prepared according to general procedure (B) using tetrahydroquinoline pyrimidine **1k** (91 mg, 0.25 mmol), halogenating source F (41 mg, 1.0 equiv). The crude reaction mixture was



purified by column chromatography using 50% EtOAc/Hexane afforded **7k** (25 mg, 22%) as a white solid. Rf: 0.53 (silica gel, 60% EtOAc/Hexane); **M. P.:** 203-208 °C; **IR (in CHCl₃, cm⁻¹):** ν_{max} : 2860, 1576, 1453, 1352, 1152, 1073, 883, 664; **¹H NMR (400 MHz, CDCl₃):** δ 8.38 (d, J = 4.8 Hz, 2H), 7.75 (d, J = 1.8 Hz, 1H), 7.45 (d, J = 1.2 Hz, 1H), 6.71 (t, J = 4.7 Hz, 1H), 4.02 (t, J = 6.6 Hz, 2H),

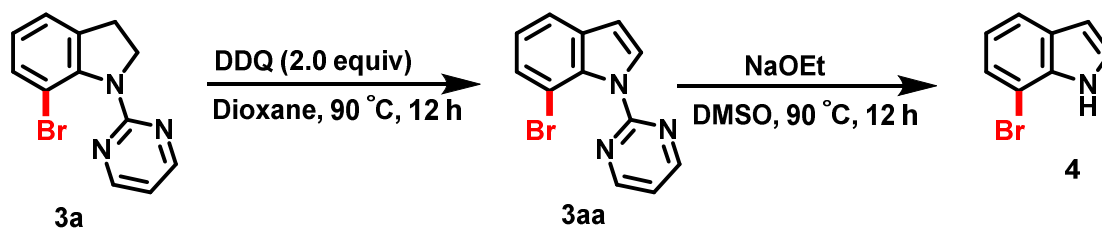
3.79–3.61 (m, 4H), 3.09–2.91 (m, 4H), 2.78 (t, J = 6.6 Hz, 2H), 2.04–1.88 (m, 2H); **¹³C NMR (100 MHz, CDCl₃):** δ 160.9, 157.7, 144.6, 136.5, 131.3, 130.4, 126.9, 121.5, 113.4, 66.1, 46.0, 45.9, 27.5, 4309; **HRMS (ESI) m/z:** [M+2+H]⁺ calcd for C₁₇H₂₀BrN₄O₃S 441.0414; Found 441.0405.

Procedure for 1.18 mmol scale of 6a: To a solution of **5a** (250 mg, 1.18 mmol) in DCE (6 mL), Pd(OAc)₂ (26 mg, 10 mol%), **C** (190 mg, 1.2 equiv) and CuO (93 mg, 1 equiv) was added in a sealed tube vial and the reaction mixture was kept in preheated oil bath at 90 °C for 24 hours. After completion of the reaction, the reaction mixture was filtered thorough short pad silica and washes with DCM. The crude reaction mixture was purified by column chromatography using 12% EtOAc/Hexane afforded **7a** (237 mg, 81%) as a colourless oil.

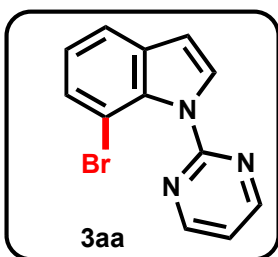
Procedure for 2.36 mmol scale of 7a: To a solution of **5a** (500 mg, 2.36 mmol) in DCE (10 mL), Pd(OAc)₂ (52 mg, 10 mol%), **F** (387 mg, 1 equiv) and CuO (375 mg, 2 equiv) was

added in a sealed tube vial and the reaction mixture was kept in preheated oil bath at 90 °C for 12 hours. After completion of the reaction, the reaction mixture was filtered through short pad silica and washes with DCM. The crude reaction mixture was purified by column chromatography using 10% EtOAc/Hexane afforded **7a** (512 mg, 75%) as a white solid.

Synthetic application:



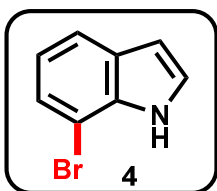
7-bromo-1-(pyrimidin-2-yl)-1H-indole (3aa): To a sealed tube vial containing **3a** (300 mg, 1.09 mmol) and DDQ (500 mg, 2.20 mmol), 1,4-dioxane (8.0 mL) was added. The mixture was stirred at 90 °C for 12 h. After completion of the reaction, the solvent was removed under reduced pressure and the residue was purified by column chromatography with 6%



EtOAc/Hexane to give indole pyrimidine **3aa** (187 mg, 63%) as a white solid. **R_f**: 0.63 (silica gel, 20% EtOAc/Hexane); **M. P.**: 87–92 °C **IR (in CHCl₃, cm⁻¹):** ν_{max} ; 1214, 742, 667; **¹H NMR (400 MHz, CDCl₃):** 8.81 (d, $J = 4.8$ Hz, 2H), 7.69 (d, $J = 3.4$ Hz, 1H), 7.61 (dd, $J = 7.7$ Hz, 0.8 Hz, 1H), 7.50 (dd, $J = 7.7$ Hz, 0.6 Hz, 1H), 7.23 (t, $J = 4.8$ Hz, 1H), 7.08 (t, $J = 4.7$ Hz, 1H), 6.71 (d, $J = 3.4$ Hz, 1H); **¹³C NMR (100 MHz, CDCl₃):** 158.3, 157.1, 133.5, 130.8, 128.7, 122.9, 120.3, 118.3, 106.6, 106.2; **HRMS (ESI) m/z:**

[M + H]⁺ Calcd for C₁₂H₉BrN₃ 273.9974; Found 273.9978.

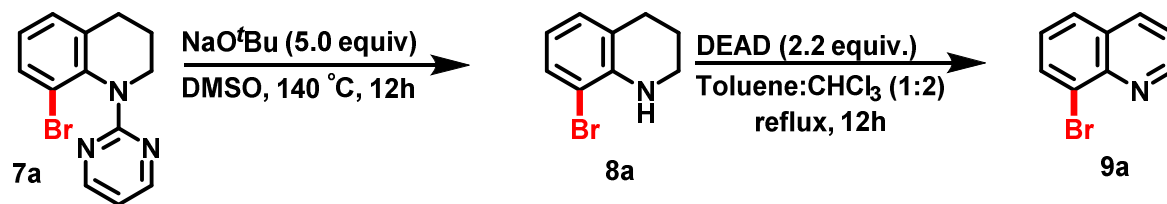
7-bromo-1H-indole (4): To a dried sealed tube vial **3aa** (30 mg, 0.11 mmol), freshly prepared 20% NaOEt in ethanol (150 μL) in dimethyl sulfoxide (2 ml) under argon atmosphere was taken;



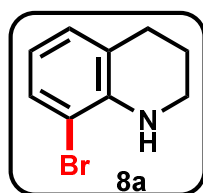
reaction mixture was kept at 90 °C for 5 h. After cooling to ambient temperature, the reaction mixture was neutralized with 1N HCl at 0 °C, the reaction mixture was diluted with Ethyl Acetate (15 mL). The filtrate was concentrated and the crude residue was purified by column chromatography

on silica gel (6% Ethyl Acetate Hexane) to give 7-bromoindole **4** (17 mg, 79%) as yellow oil. **R_f**: 0.67 (silica gel, 20% EtOAc/Hexane); **IR (in CHCl₃, cm⁻¹):** ν_{max} ; 3018, 1562, 1483, 1407, 1330, 1214, 1191, 1094, 920, 742; **¹H NMR in CDCl₃ (400 MHz):** 8.32 (s, 1H), 7.57 (d, $J = 7.9$ Hz,

1H), 7.32 (dd, $J = 7.6$ Hz, 0.4 Hz, 1H), 7.26–7.22 (m, 1H), 6.99 (t, $J = 7.8$ Hz, 1H), 6.62 (dd, $J = 3.2$ Hz, 2.2 Hz, 1H); ^{13}C NMR in CDCl_3 (100 MHz): 134.5, 128.9, 124.6, 124.3, 120.9, 119.9, 104.6, 103.8; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_8\text{H}_7\text{BrN}$ 195.9756; Found 195.9756.



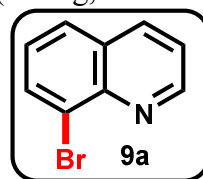
8-bromo-1,2,3,4-tetrahydroquinoline (8a): To a dried sealed tube vial **7a** (140 mg, 0.5 mmol), ^tBuONa (240 mg, 2.5 mmol) in dimethyl sulfoxide (3 mL) under argon atmosphere was taken;



reaction mixture was kept at 140 °C for 12 h. After cooling to ambient temperature, the reaction mixture was neutralized with 1N HCl at 0 °C, the reaction mixture was diluted with Ethyl Acetate (15 mL). The filtrate was concentrated and the crude residue was purified by column chromatography

on silica gel (5% Ethyl Acetate Hexane) to give **8a** (57 mg, 54%) as colourless liquid. R_f : 0.70 (silica gel, 10% EtOAc/Hexane); IR (in CHCl_3 , cm^{-1}): ν_{max} ; 3648, 3360, 2926, 2360, 1868, 1584, 1457, 1159, 626; ^1H NMR in CDCl_3 (400 MHz): 7.23 (dd, $J = 7.9$ Hz, 1.4 Hz, 1H), 6.89 (dd, $J = 7.3$ Hz, 1.3 Hz, 1H), 6.45 (t, $J = 7.6$ Hz, 1H), 4.42 (s, 1H), 3.39 (t, $J = 4.6$, 2H), 2.77 (t, $J = 6.5$, 2H), 1.99–1.86 (m, 2H); ^{13}C NMR in CDCl_3 (100 MHz): 141.6, 129.9, 128.3, 122.8, 116.8, 108.6, 42.0, 27.4, 21.6; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_9\text{H}_{11}\text{BrN}$ 212.0069; Found 212.0071.

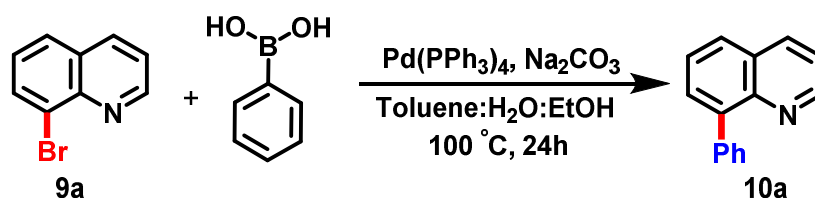
8-bromoquinoline (9a):⁵ To a sealed tube vial containing **8a** (50 mg, 0.23 mmol) and DEAD (91 mg, 0.52 mmol), chloroform (0.25 mL) and toluene (0.5 mL) was added. The mixture was



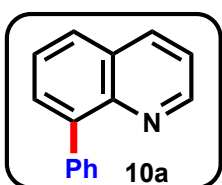
reflux for 12 h. After completion of the reaction, the reaction mixture was directly subjected for column chromatography 5% EtOAc/Hexane to give **9a** (30 mg, 61%) as a yellow oil. R_f : 0.50 (silica gel, 10% EtOAc/Hexane); IR

(in CHCl_3 , cm^{-1}): ν_{max} ; 2982, 1592, 1491, 1383, 1306, 1214, 1062, 996, 741; ^1H NMR (400 MHz, CDCl_3): 9.06 (dd, $J = 4.2$ Hz, 1.7 Hz, 1H), 8.18 (dd, $J = 8.2$ Hz, 1.6 Hz, 1H), 8.07 (dd, $J = 7.4$ Hz, 1.2 Hz, 1H), 7.81 (dd, $J = 8.1$ Hz, 1.2 Hz, 1H), 7.48 (dd, $J = 8.2$ Hz, 4.2 Hz, 1H), 7.41 (t, $J = 7.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): 151.2, 145.3, 136.6, 133.2, 129.5, 127.6,

126.9, 124.7, 121.9; **HRMS (ESI)** m/z : $[M + H]^+$ Calcd for C_9H_7BrN 207.9756; Found 207.9760.

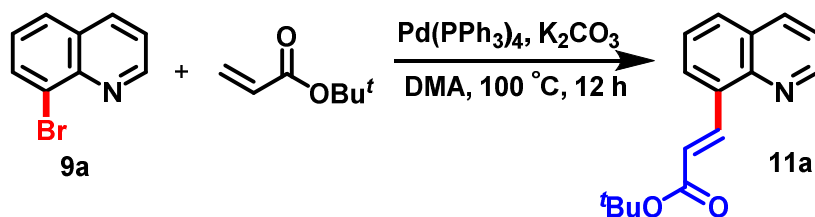


8-phenylquinoline (10a): To a mixture of **9a** (30 mg, 0.15 mmol), sodium carbonate (31 mg, 0.29 mmol), phenylboronic acid (26 mg, 0.21 mmol) and $Pd(PPh_3)_4$ (17 mg, 0.015 mmol) in

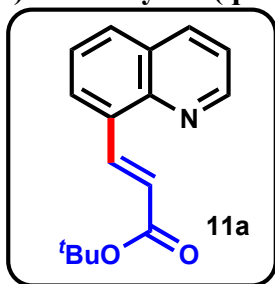


toluene:water:ethanol (5:5:1) 2 mL was taken under argon atmosphere in a sealed tube vial. The reaction mixture was stirred at 100 °C for 24 h in oil bath. The reaction mixture was extracted with ethyl acetate (10 mL X 2), dried over Na_2SO_4 , concentrated via rotavapor and subjected for column

chromatography to afford product **10a** (26 mg, 85%) as yellow colour liquid. R_f : 0.50 (silica gel, 40% EtOAc/Hexane); **IR (in $CHCl_3$, cm^{-1})**: ν_{max} : 3018, 1731, 1595, 1494, 1445, 1374, 1214, 1045, 996; **1H NMR (400 MHz, $CDCl_3$)**: 1H NMR in $CDCl_3$ (400 MHz): 8.96 (dd, $J = 4.0$ Hz, 1.5 Hz, 1H), 8.20 (dd, $J = 8.3$ Hz, 1.8 Hz, 1H), 7.83 (dd, $J = 8.1$ Hz, 1.3 Hz, 1H), 7.77–7.67 (m, 3H), 7.61 (t, $J = 7.5$ Hz, 1H), 7.55–7.46 (m, 2H), 7.46–7.38 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)**: 150.2, 146.0, 140.9, 139.5, 136.2, 130.6, 130.3, 128.7, 127.9, 127.5, 127.3, 126.2, 120.9; **HRMS (ESI)** m/z : $[M + H]^+$ Calcd for $C_{15}H_{12}N$ 206.0964; Found 206.0952.

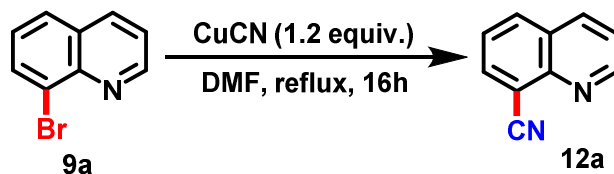


(*E*)-*tert*-butyl 3-(quinolin-8-yl)acrylate (**11a**): To a mixture of **9a** (30 mg, 0.15 mmol),

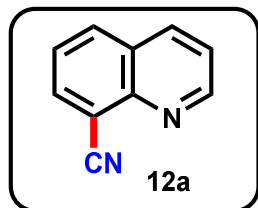


potassium carbonate (41 mg, 0.3 mmol), *tert*-Butylacrylate (57 mg, 0.45 mmol) and Pd(PPh₃)₄ (17 mg, 0.015) in DMA 1 mL was taken under argon atmosphere in a sealed tube vial. The reaction mixture was stirred at 100 °C for 24 h in oil bath. The reaction mixture directly subjected for column chromatography to afford product **11a** (22 mg, 58%) as

colourless liquid. *R_f*: 0.50 (silica gel, 20% EtOAc/Hexane); IR (in CHCl₃, cm⁻¹): *v*_{max}; 2981, 1698, 1633, 1594, 1573, 1456, 1368, 1233, 1152, 1044, 985; ¹H NMR (400 MHz, CDCl₃): ¹H NMR in CDCl₃ (400 MHz): 8.97 (dd, *J* = 4.1 Hz, 1.8 Hz, 1H), 8.80 (d, *J* = 16.3 Hz, 1H), 8.15 (dd, *J* = 8.2 Hz, 1.8 Hz, 1H), 7.95 (dd, *J* = 7.2 Hz, 0.2 Hz, 1H), 7.83 (dd, *J* = 8.2 Hz, 1.3 Hz, 1H), 7.54 (t, *J* = 7.7 Hz, 1H), 7.44 (dd, *J* = 8.3 Hz, 4.1 Hz, 1H), 6.74 (d, *J* = 16.2 Hz, 1H), 1.57 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): 166.4, 150.1, 146.2, 139.9, 136.2, 133.5, 129.6, 128.4, 127.9, 126.2, 122.7, 121.4, 80.4, 28.2; HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₆H₁₈NO₂ 256.1332; Found 256.1330.

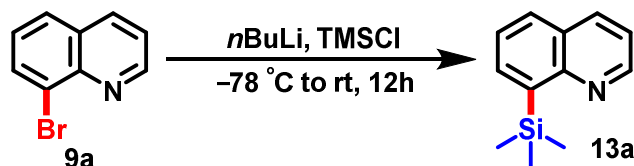


quinoline-8-carbonitrile (**12a**): To a mixture of **9a** (30 mg, 0.15 mmol), CuCN (16 mg, 0.17 mmol) in DMF 1 mL was taken under in a sealed tube vial. The reaction mixture was stirred

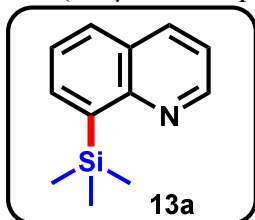


reflux for 16 h in oil bath. The reaction mixture purified by preparative TLC afford product **12a** (12 mg, 53%) as white solid. *R_f*: 0.55 (silica gel, 30% EtOAc/Hexane); M. P.: 110-115 °C; IR (in CHCl₃, cm⁻¹): *v*_{max}; 1214, 742, 667; ¹H NMR (400 MHz, CDCl₃): ¹H NMR in CDCl₃ (400

MHz): 9.12 (dd, *J* = 4.2 Hz, 1.7 Hz, 1H), 8.25 (dd, *J* = 8.3 Hz, 1.7 Hz, 1H), 8.15 (dd, *J* = 7.2 Hz, 1.3 Hz, 1H), 8.05 (dd, *J* = 8.2 Hz, 1.4 Hz, 1H), 7.63 (dd, *J* = 8.2 Hz, 7.2 Hz, 1H), 7.57 (dd, *J* = 8.3 Hz, 4.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): 152.5, 147.5, 136.4, 135.5, 132.8, 128.2, 125.9, 122.8, 117.2, 113.3; HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₀H₇N₂ 155.0604; Found 155.0604.

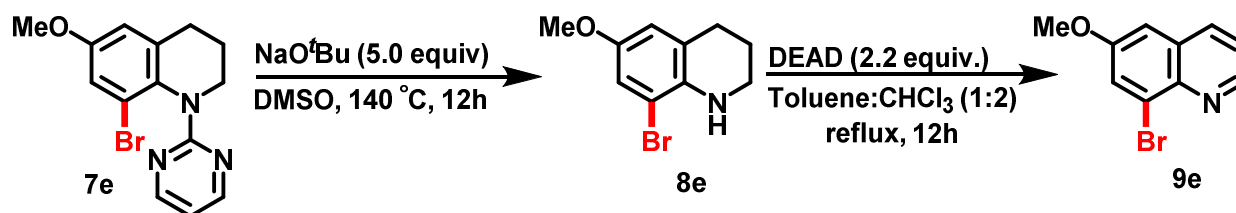


8-(trimethylsilyl)quinoline (13a):⁷ To a mixture of **9a** (30 mg, 0.15 mmol), *n*BuLi 1.5 M in THF (87 μ L 1.2 equiv.) in THF 1 mL was taken at -78 $^{\circ}$ C under argon atmosphere in 10 ml

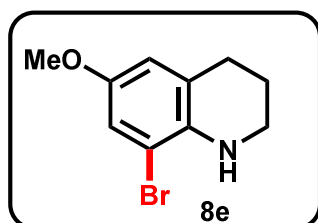


flask. The reaction mixture was stirred at that temperature for 5 minutes and trimethylsilyl chloride (20 μ L 1.2 equiv.) was added then reaction kept at room temperature for 12 h. The reaction mixture was purified by column chromatography afford product **13a** (24 mg, 82%) as yellow

liquid. *R*_f: 0.8 (silica gel, Hexane); **IR (in CHCl₃, cm⁻¹):** ν_{max} ; 1232, 797, 707; **¹H NMR (400 MHz, CDCl₃):** ¹H NMR in CDCl₃ (400 MHz): 8.90 (dd, *J* = 4.2 Hz, 1.8 Hz, 1H), 8.11 (dd, *J* = 8.2 Hz, 1.8 Hz, 1H), 7.87 (dd, *J* = 6.7 Hz, 1.5 Hz, 1H), 7.80 (dd, *J* = 8.1 Hz, 1.4 Hz, 1H), 7.50 (dd, *J* = 8.0 Hz, 6.7 Hz, 1H), 7.35 (dd, *J* = 8.2 Hz, 4.1 Hz, 1H), 0.45 (s, 9H); **¹³C NMR (100 MHz, CDCl₃):** 152.6, 149.0, 141.7, 136.0, 136.5, 129.0, 127.6, 125.9, 120.6, -0.29; **HRMS (ESI) m/z: [M + H]⁺** Calcd for C₁₂H₁₆NSi 202.1047; Found 202.1048.



8-bromo-6-methoxy-1,2,3,4-tetrahydroquinoline (8e): To a dried sealed tube vial **7e** (200 mg,

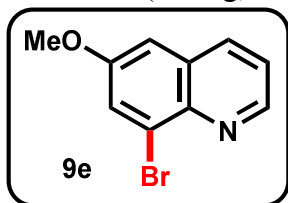


0.62 mmol), ^tBuONa (300 mg, 3.1 mmol) in dimethyl sulfoxide (5 mL) under argon atmosphere was taken; reaction mixture was kept at 140 $^{\circ}$ C for 12 h. After cooling to ambient temperature, the reaction mixture was neutralized with 1N HCl at 0 $^{\circ}$ C, the reaction mixture

was diluted with Ethyl Acetate (15 mL). The filtrate was concentrated and the crude residue was purified by column chromatography on silica gel (5% Ethyl Acetate Hexane) to give **8e** (60 mg, 40%) as yellow liquid. *R*_f: 0.70 (silica gel, 10% EtOAc/Hexane); **IR (in CHCl₃, cm⁻¹):** ν_{max} ; 3355, 2044, 1735, 1649, 1496, 1439, 1419, 1253, 1107, 1044, 661; **¹H NMR in CDCl₃ (400 MHz):** 6.87 (d, *J* = 2.8 Hz, 1H), 6.54 (d, *J* = 2.8 Hz, 1H), 4.08 (br s, 1H), 3.70 (s, 3H), 3.33 (t, *J* = 5.3 Hz, 2H), 2.75 (t, *J* = 6.5 Hz, 2H), 1.96–1.86 (m, 2H); **¹³C NMR in CDCl₃ (100 MHz):**

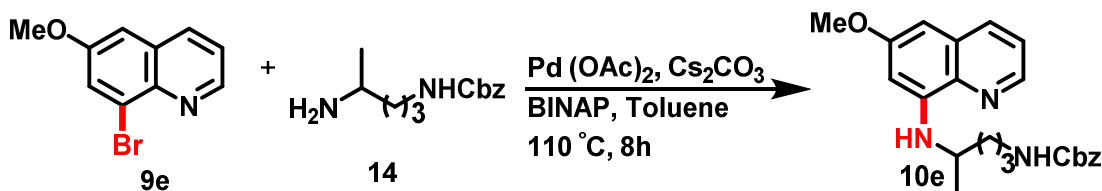
150.0, 136.2, 123.8, 115.7, 115.1, 108.8, 56.0, 42.2, 27.6, 22.0; **HRMS (ESI) m/z:** $[M + H]^+$ Calcd for $C_{10}H_{13}BrNO$ 242.0175; Found 242.0176.

8-bromo-6-methoxyquinoline (9e):⁵ To a sealed tube vial containing **8e** (50 mg, 0.207 mmol) and DEAD (90 mg, 0.51 mmol), chloroform (0.25 mL) and toluene (0.5 mL) was added. The

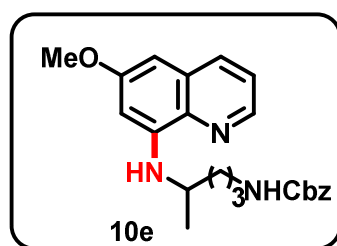


mixture was reflux for 12 h. After completion of the reaction, the reaction mixture was directly subjected for column chromatography 25% EtOAc/Hexane to give **9e** (37 mg, 75%) as a yellow oil. **R_f**: 0.50 (silica gel, 40% EtOAc/Hexane); **IR (in CHCl₃, cm⁻¹):** ν_{max} ; 2082,

1695, 15601, 1470, 1210, 1144, 1045, 996, 850; **¹H NMR (400 MHz, CDCl₃):** **¹H NMR in CDCl₃ (400 MHz):** 8.89 (dd, $J = 4.2$ Hz, 1.6 Hz, 1H), 8.03 (dd, $J = 8.2$ Hz, 1.6 Hz, 1H), 7.76 (d, $J = 2.6$ Hz, 1H), 7.40 (dd, $J = 8.2$ Hz, 4.2 Hz, 1H), 7.06 (d, $J = 2.6$, 1H), 3.92 (s, 3H); **¹³C NMR (100 MHz, CDCl₃):** 157.4, 148.7, 141.5, 135.3, 129.9, 125.7, 125.5, 122.1, 105.4, 55.8; **HRMS (ESI) m/z:** $[M + H]^+$ Calcd for $C_{10}H_9BrNO$ 237.9862; Found 237.9864.



benzyl (4-((6-methoxyquinolin-8-yl)amino)pentyl)carbamate (10e): To a mixture of **9e** (30 mg, 0.12



mmol), cesium carbonate (83 mg, 0.25 mmol), BINAP (12 mg, 0.02 mmol), and *N*-(4-aminopentyl)-4-phenylbutanamide (**14**) (36 mg, 0.15 mmol) in dry toluene (1 mL) was added Pd(OAc)₂ (3 mg, 0.013 mmol) in an oven-dried sealed tube vial under argon atmosphere. The reaction mixture was stirred at 110 °C for 8 h in oil bath. The crude reaction mixture was applied directly to a silica gel column to afford the purified

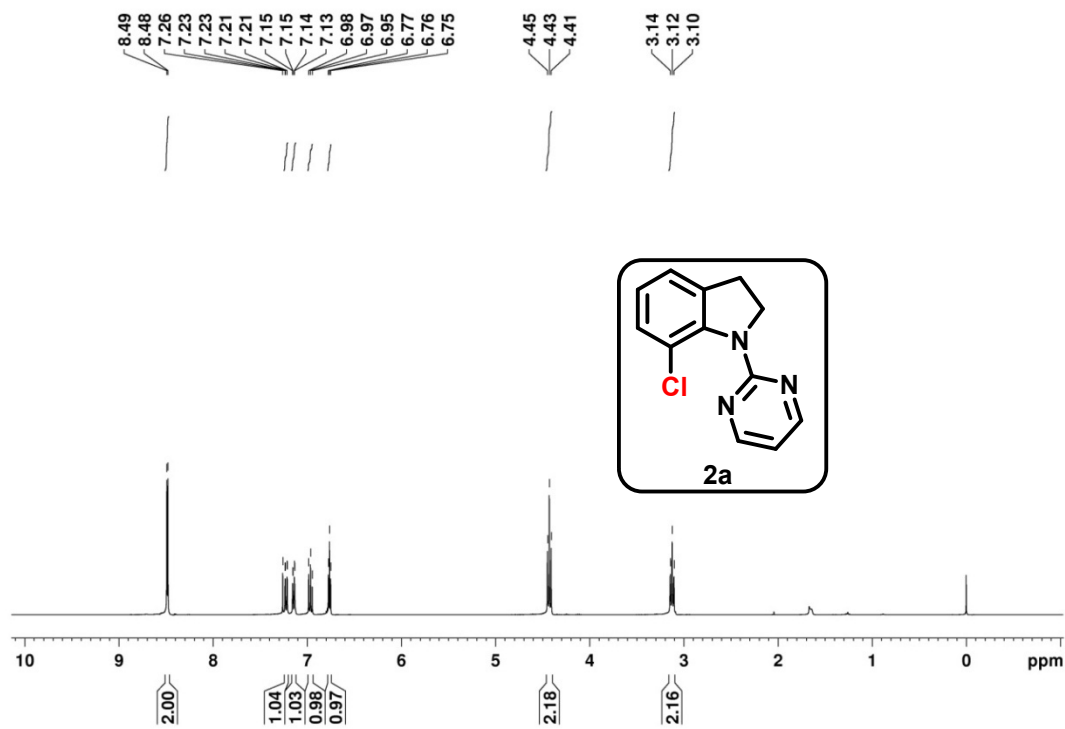
cross-coupled product **10e** (17 mg, 32%) as yellow colour liquid. **IR (in CHCl₃, cm⁻¹):** ν_{max} ; 2982, 1592, 1491, 1383, 1306, 1214, 1062, 996, 741; 3019, 1716, 1520, 1214, 908, 742; **¹H NMR (400 MHz, CDCl₃):** **¹H NMR in CDCl₃ (400 MHz):** 8.52 (dd, $J = 4.2$ Hz, 2.6 Hz, 1H), 7.91 (dd, $J = 8.2$ Hz, 1.5 Hz, 1H), 7.37–7.27 (m, 6H), 6.33 (d, $J = 2.4$ Hz, 1H), 6.27 (d, $J = 2.1$ Hz, 1H), 5.99 (d, $J = 7.9$, 1H), 5.08 (s, 2H), 4.46 (brs, 1H), 3.88 (s, 3H), 3.68–3.54 (m, 1H), 3.29–3.14 (m, 2H), 1.77–1.61 (m, 4H), 1.29 (d, $J = 6.3$ Hz, 3H); **¹³C NMR (100 MHz, CDCl₃):** 159.4, 156.4,

144.9, 144.3, 136.6, 135.4, 134.7, 129.9, 128.5, 128.0, 127.0, 121.8, 96.8, 91.7, 66.6, 55.2, 47.8, 41.1, 33.9, 26.7, 20.6; **HRMS (ESI)** m/z: [M + H]⁺ Calcd for C₂₃H₂₈N₃O₃ 394.2125; Found 394.2126.

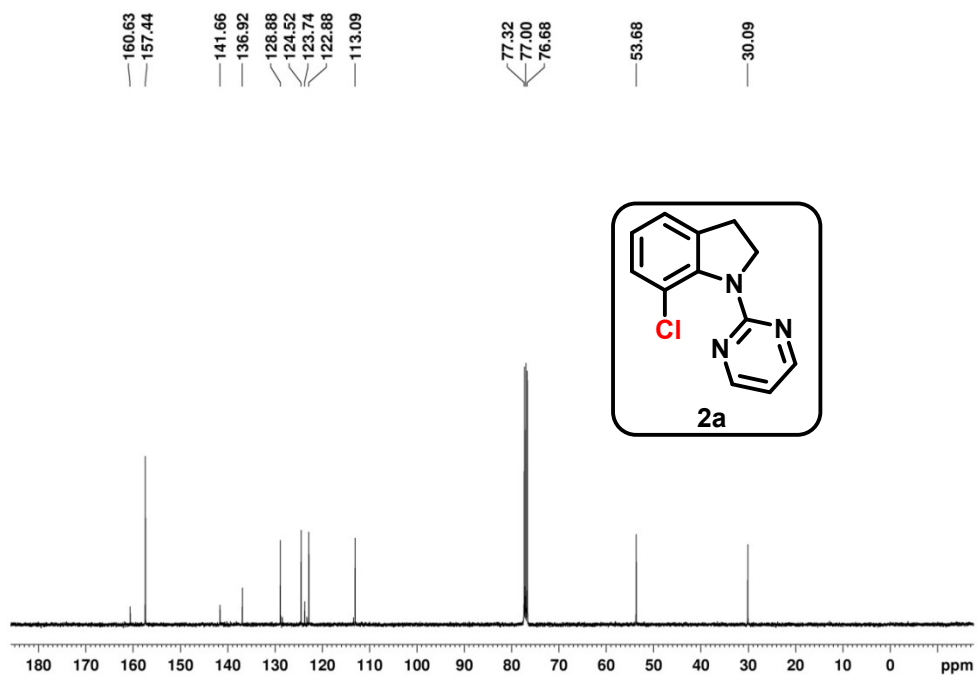
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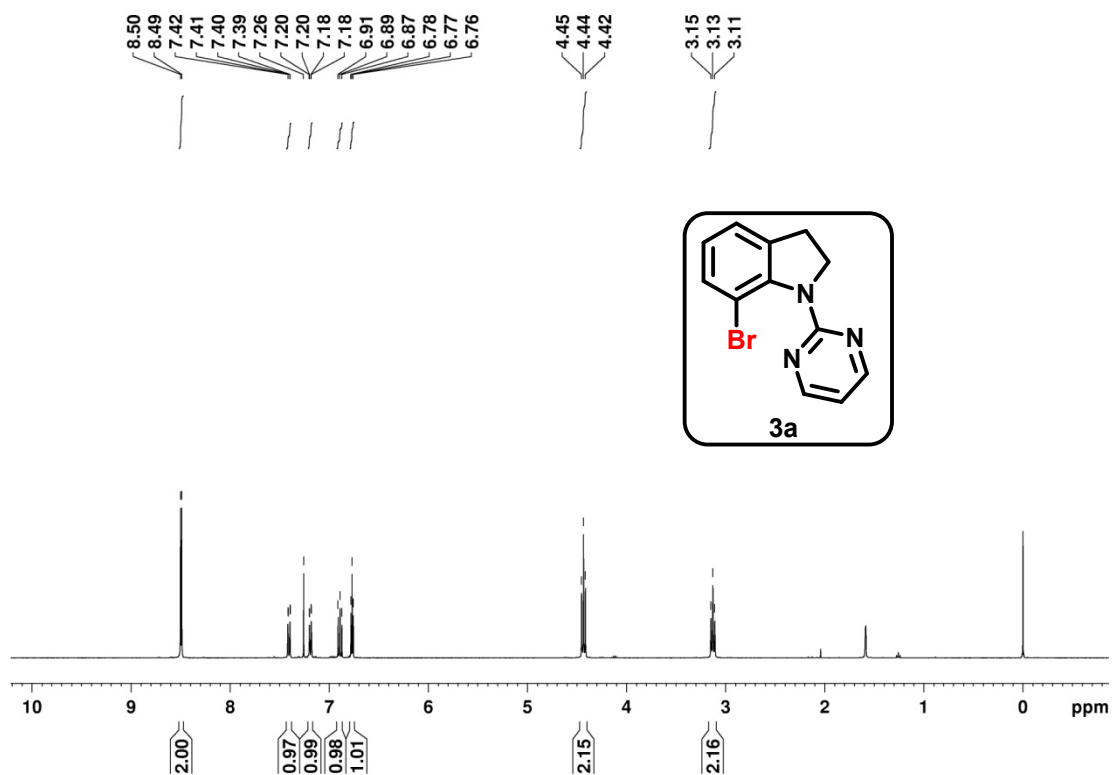
Copies of ^1H and ^{13}C NMR spectra of products:



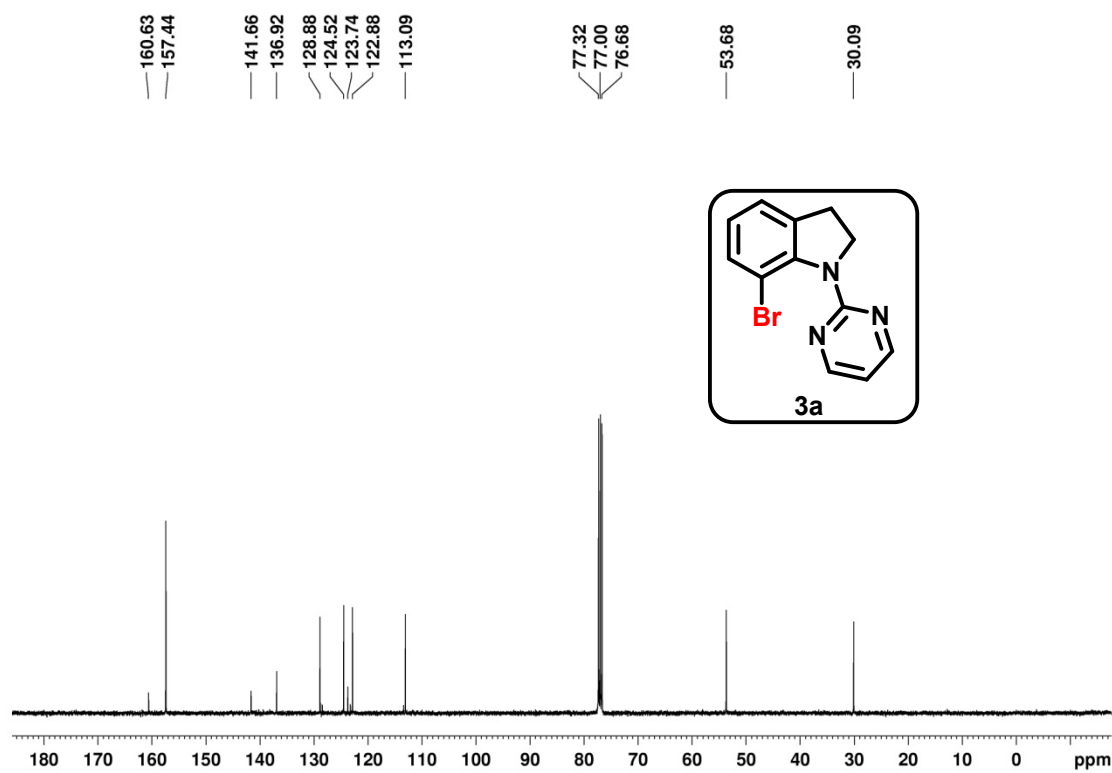
^1H NMR spectrum of **2a** (400 MHz, CDCl_3)



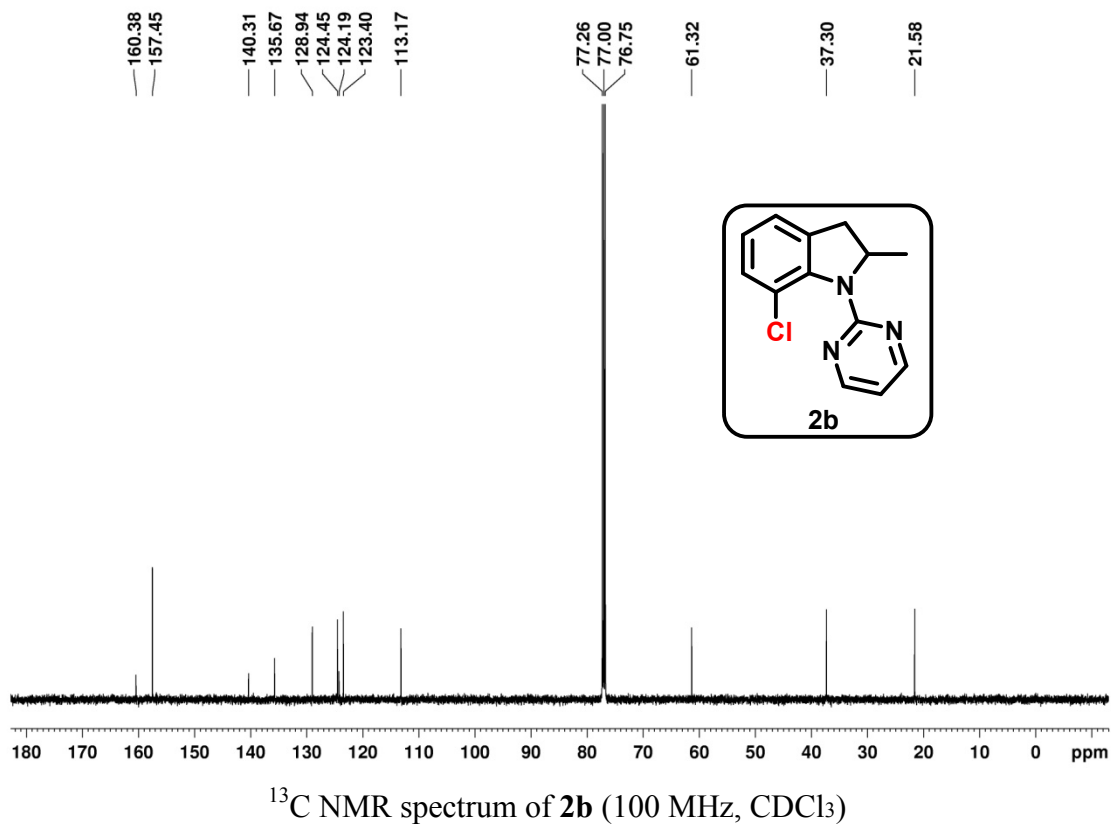
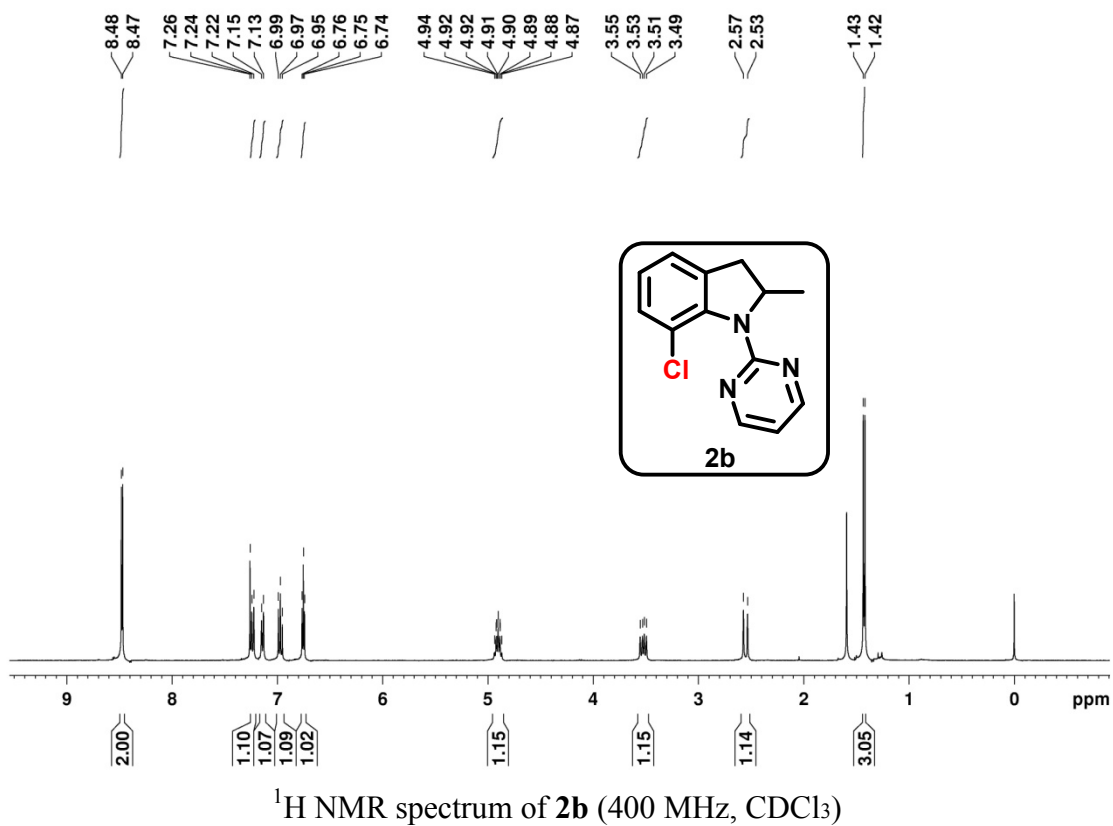
^{13}C NMR spectrum of **2a** (100 MHz, CDCl_3)

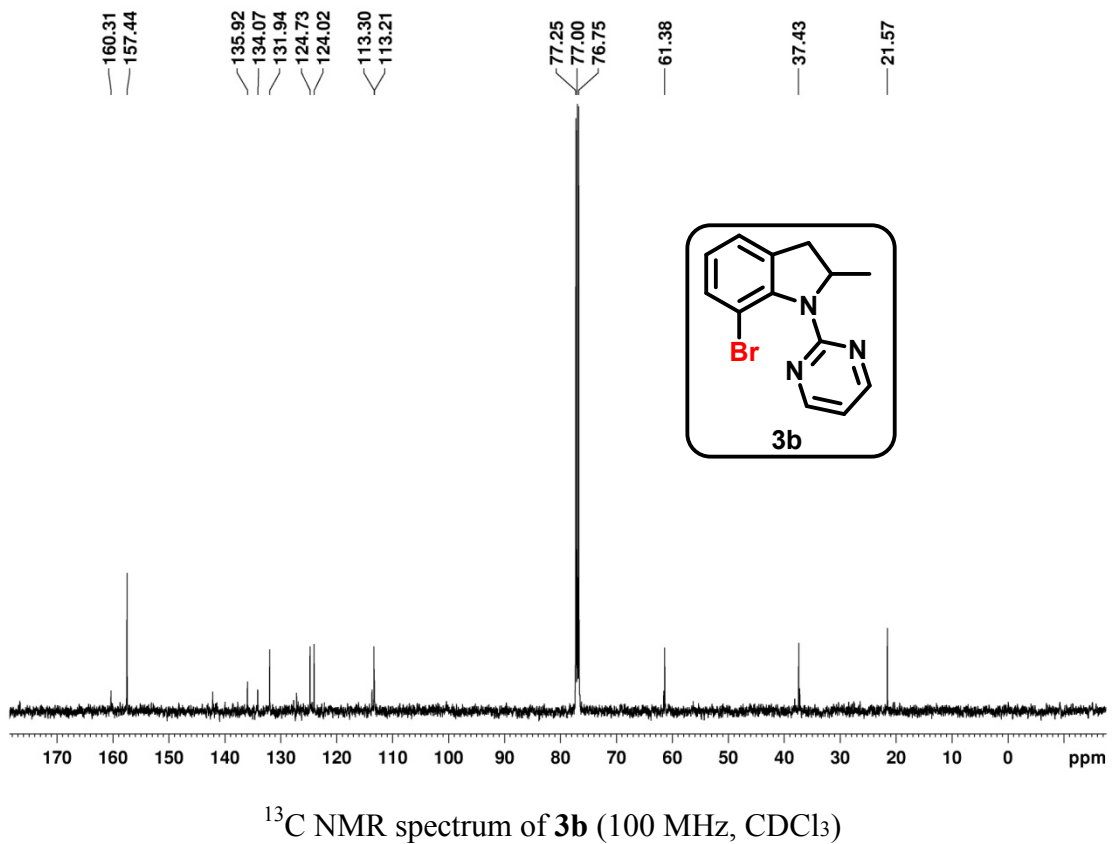
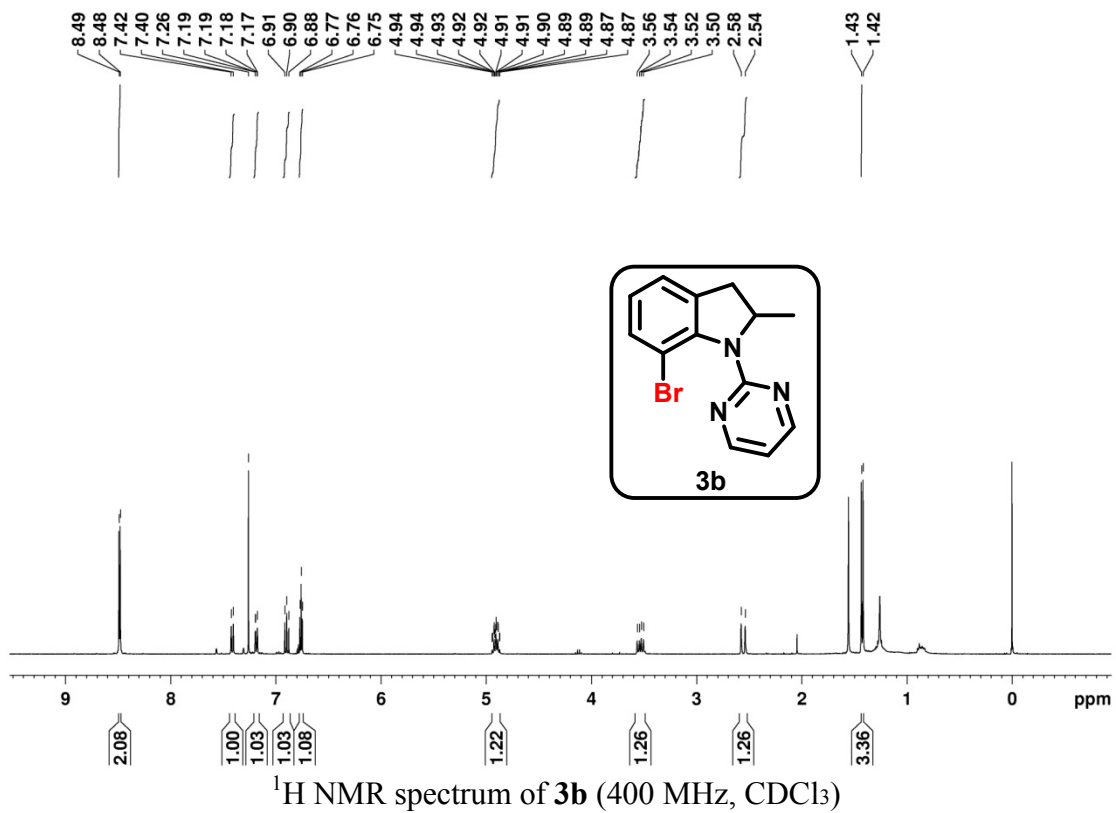


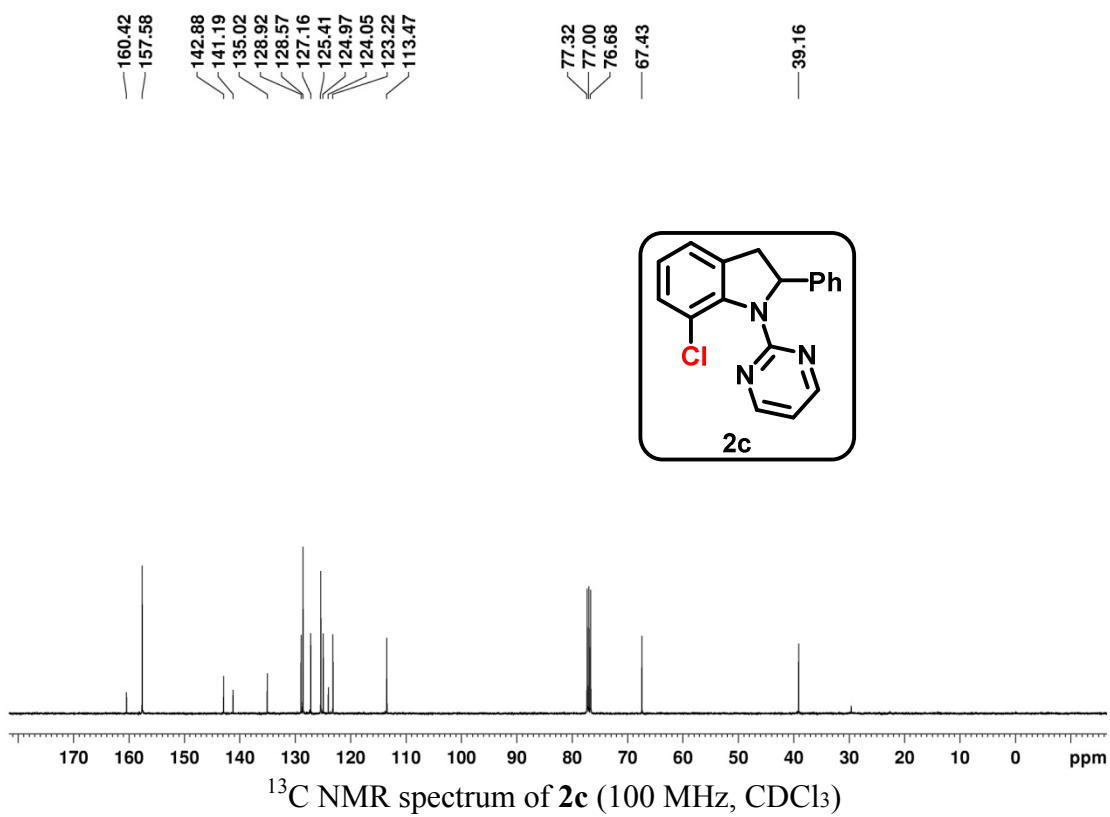
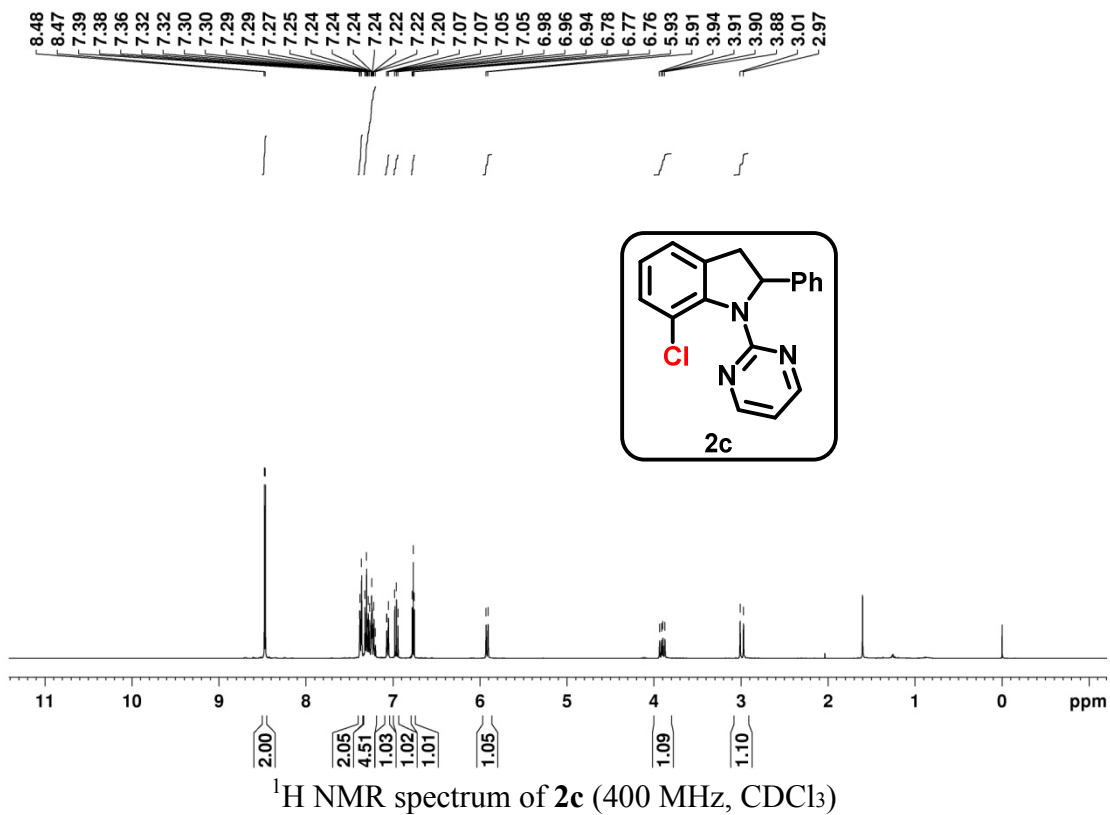
¹H NMR spectrum of **3a** (400 MHz, CDCl₃)

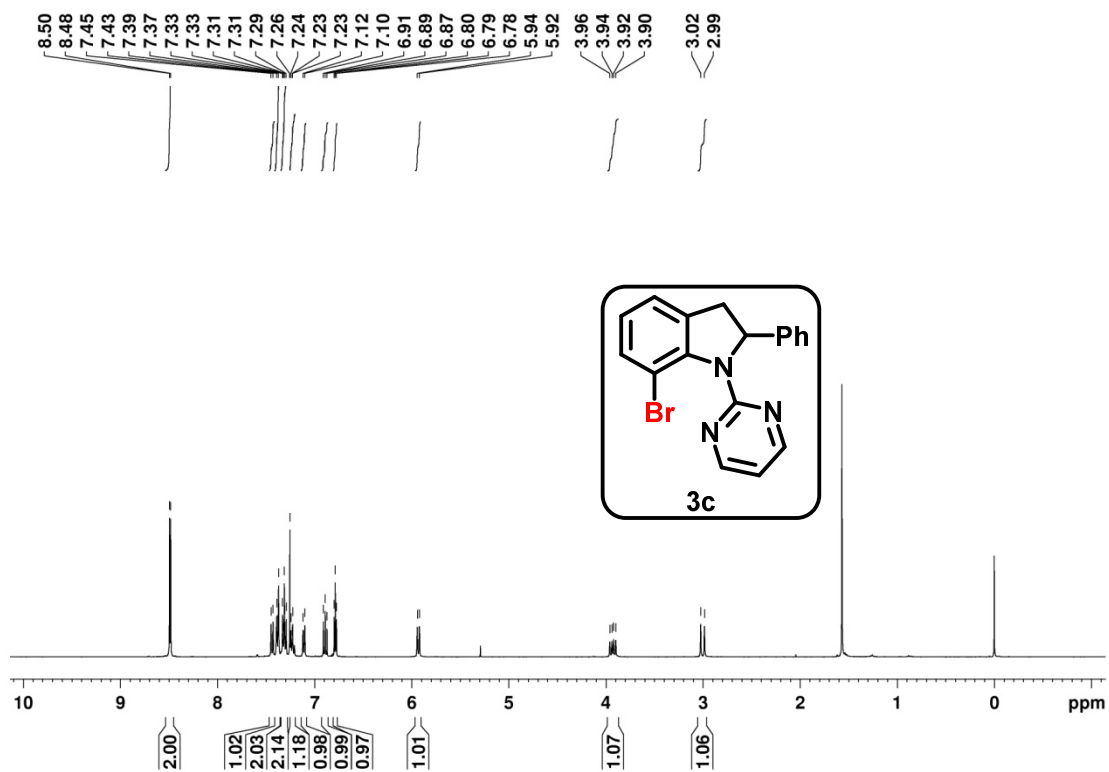


¹³C NMR spectrum of **3a** (100 MHz, CDCl₃)

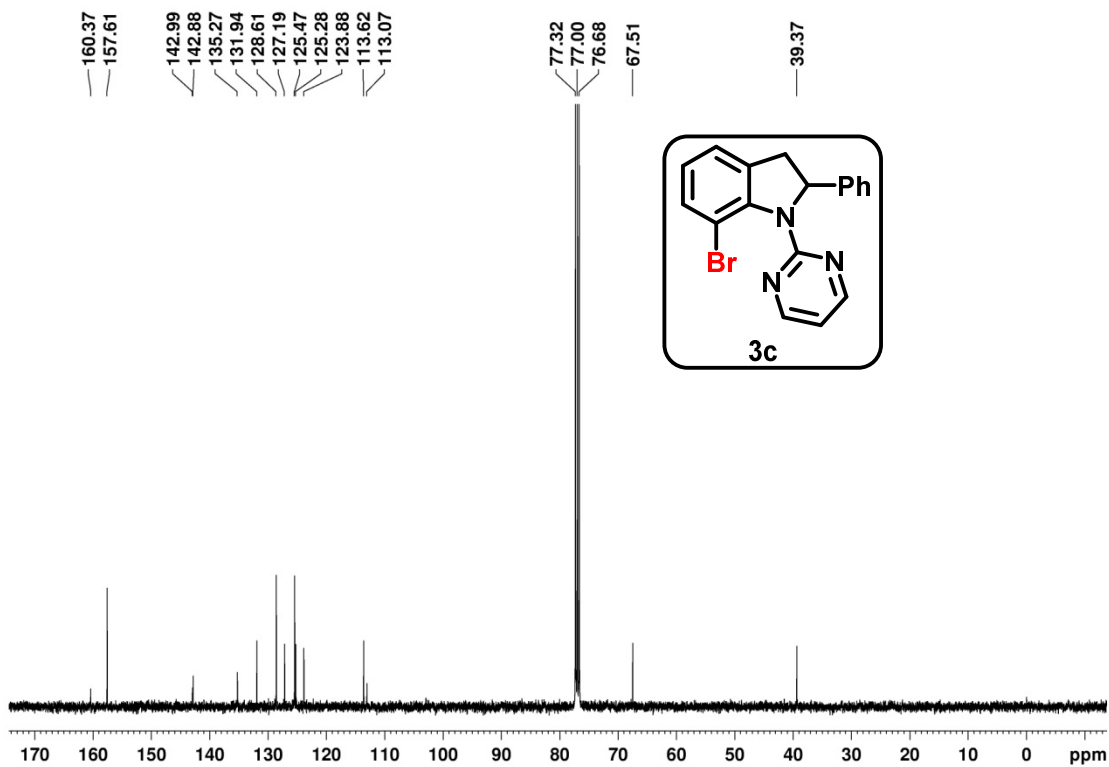




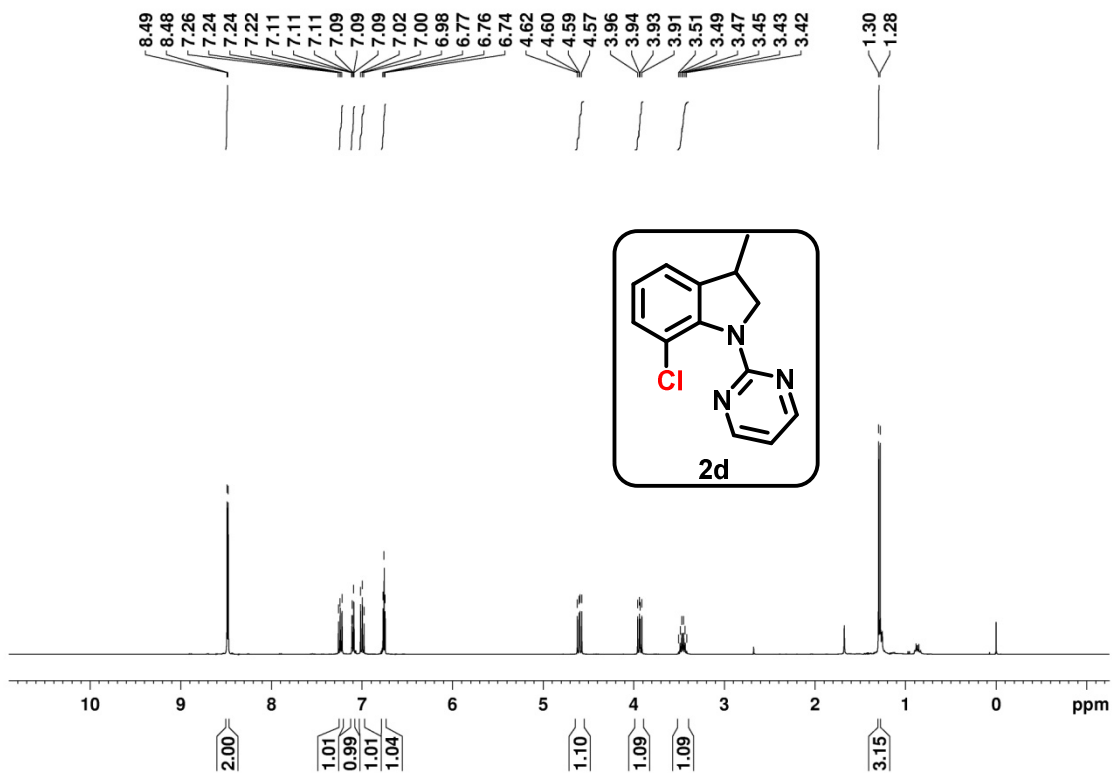




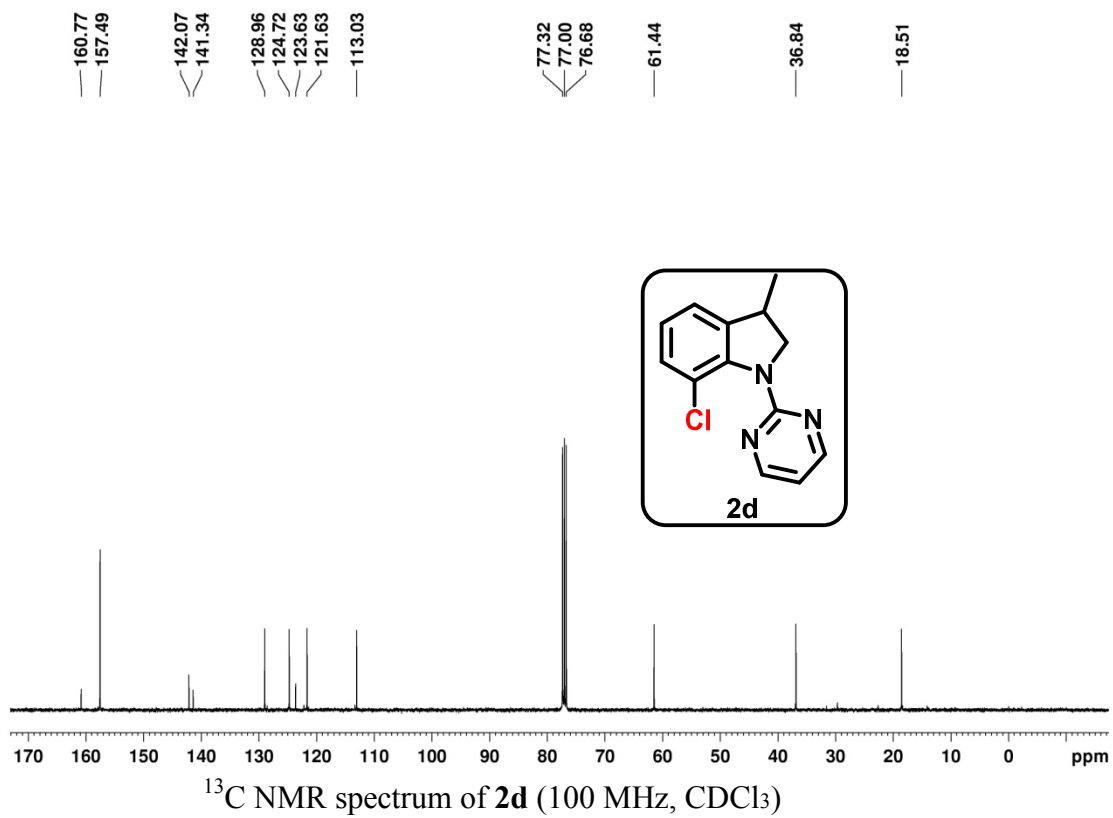
¹H NMR spectrum of **3c** (400 MHz, CDCl₃)

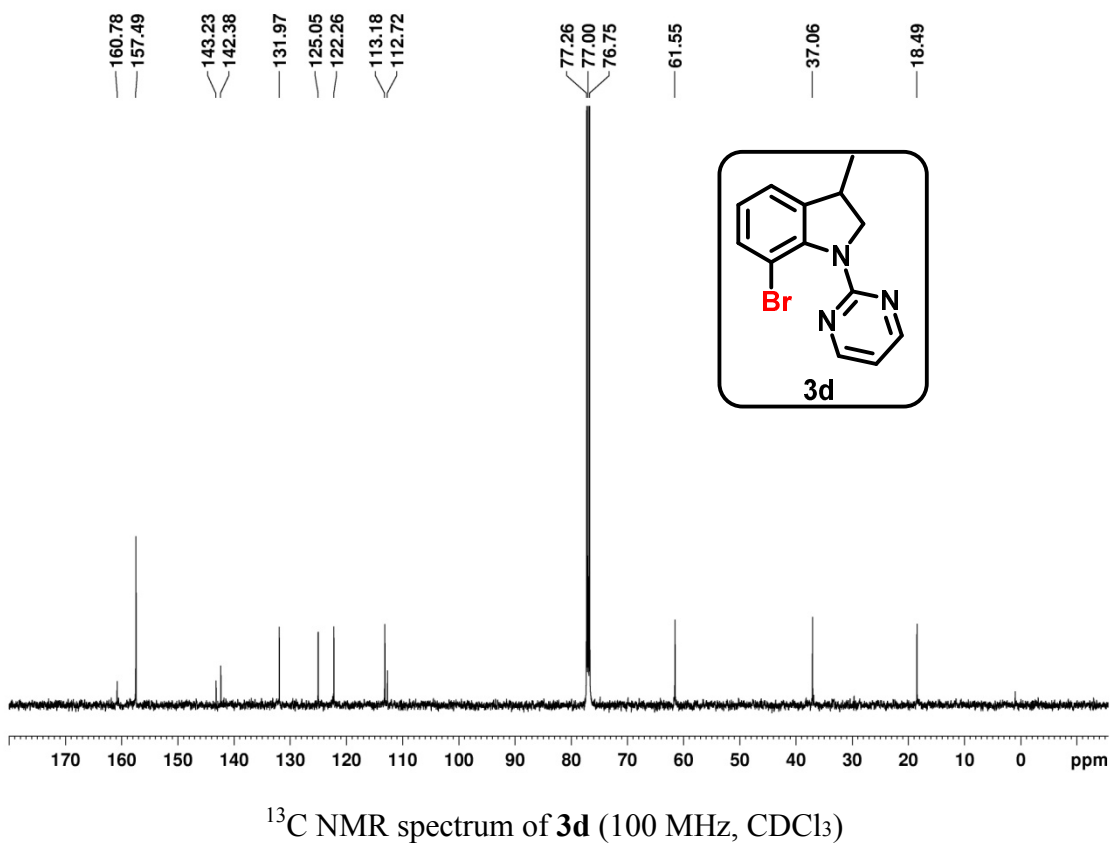
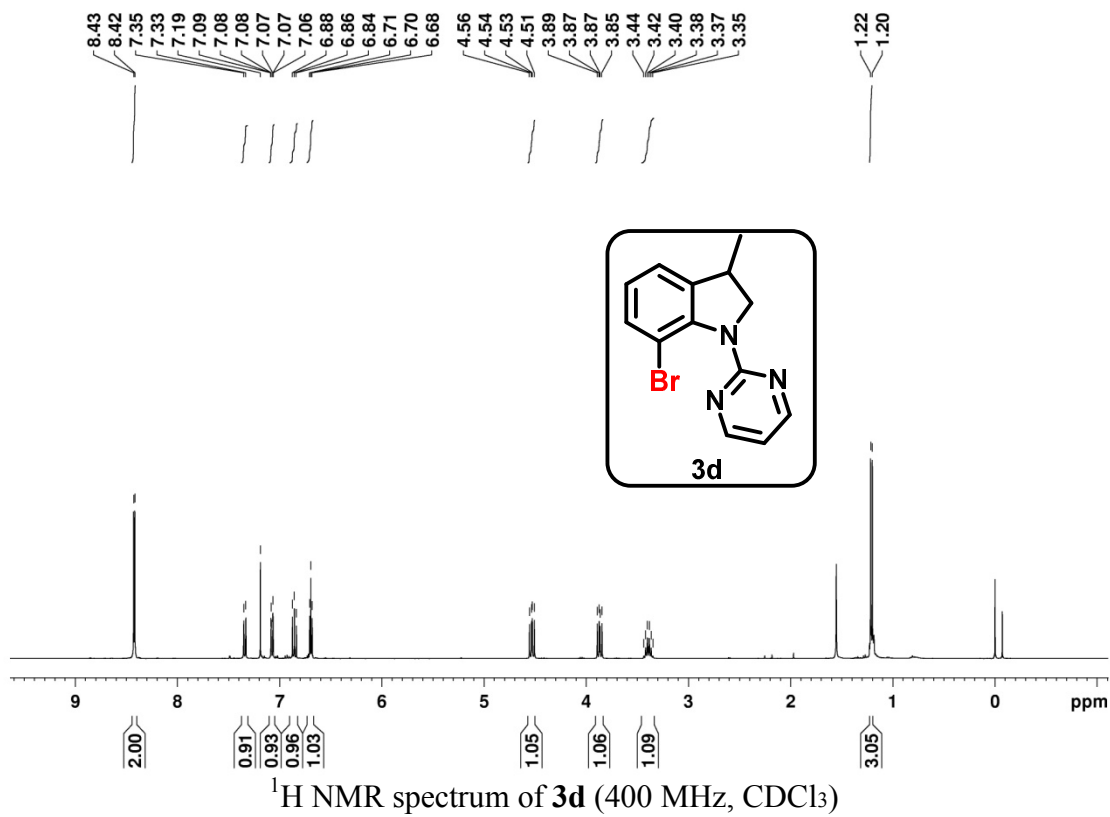


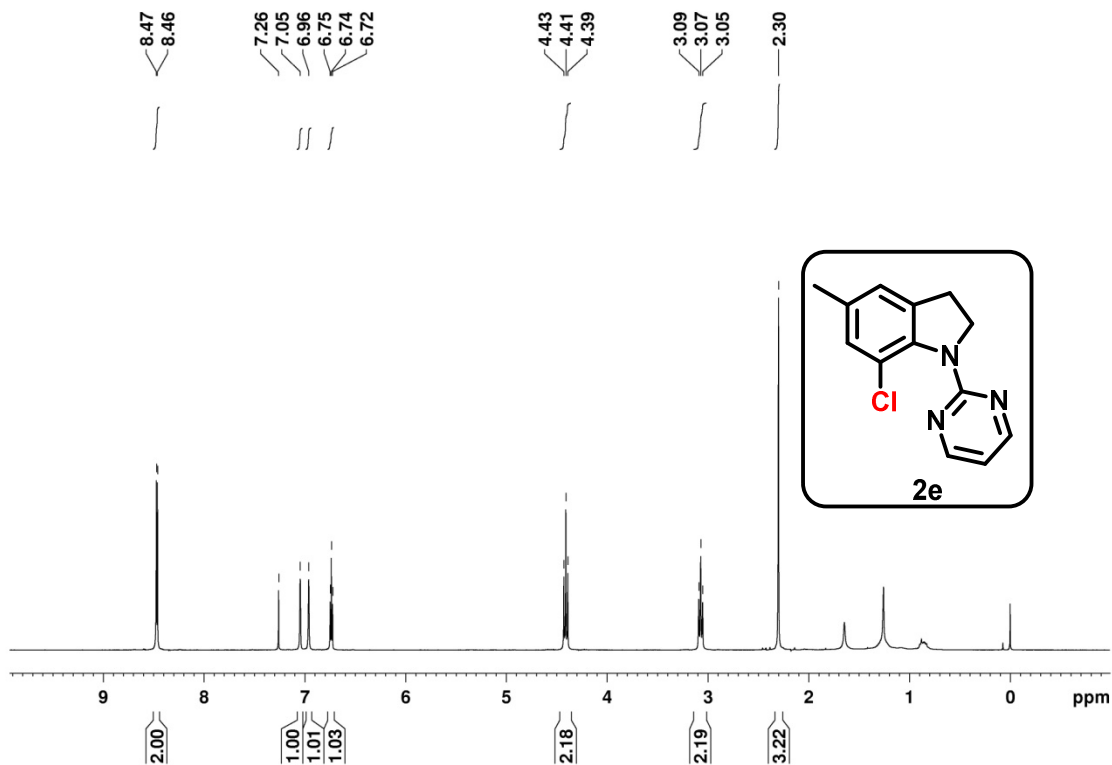
¹³C NMR spectrum of **3c** (100 MHz, CDCl₃)



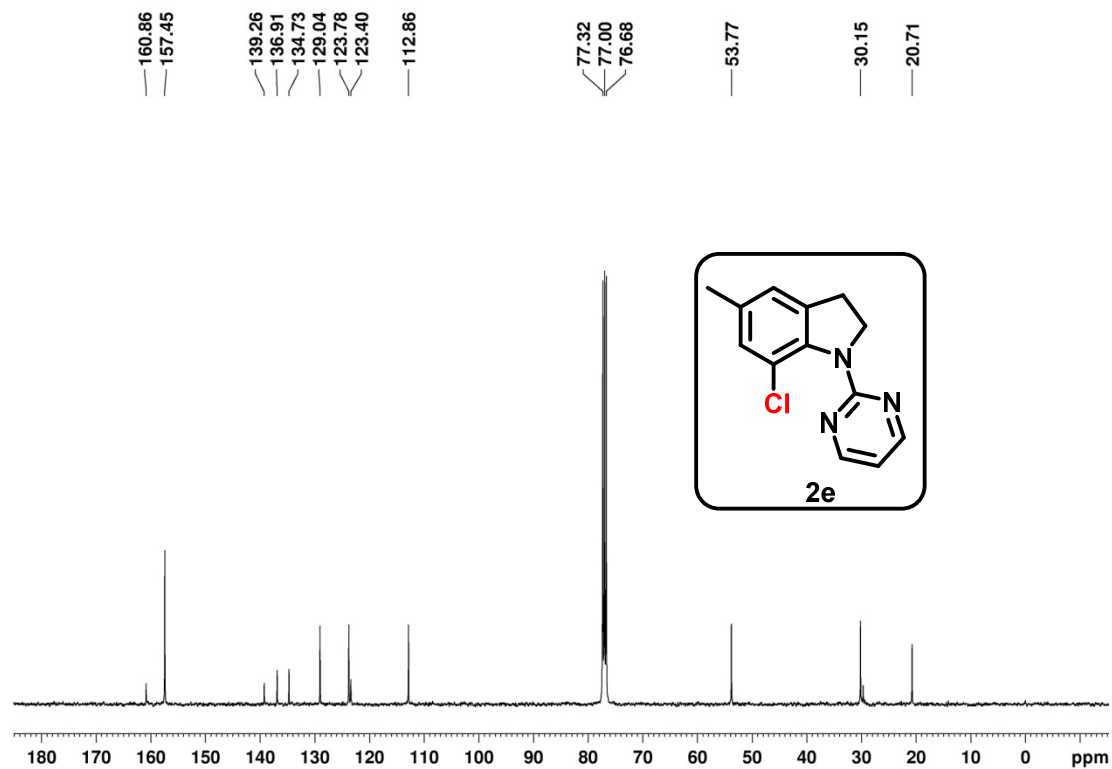
¹H NMR spectrum of **2d** (400 MHz, CDCl₃)



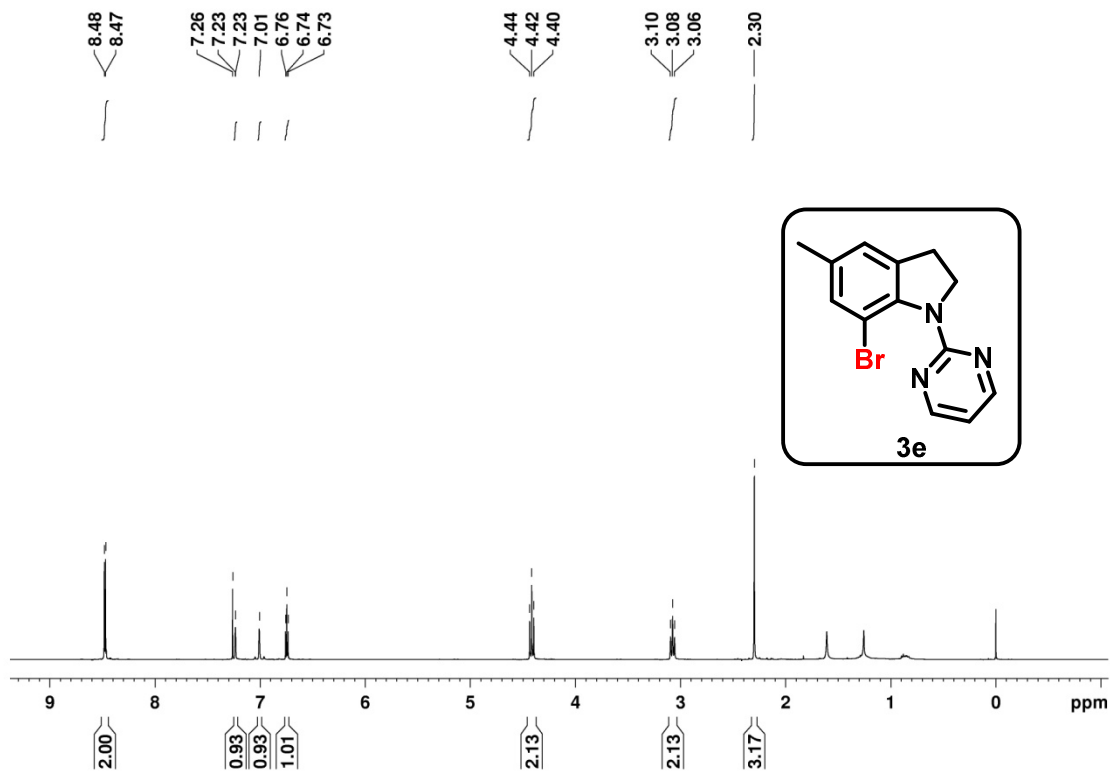




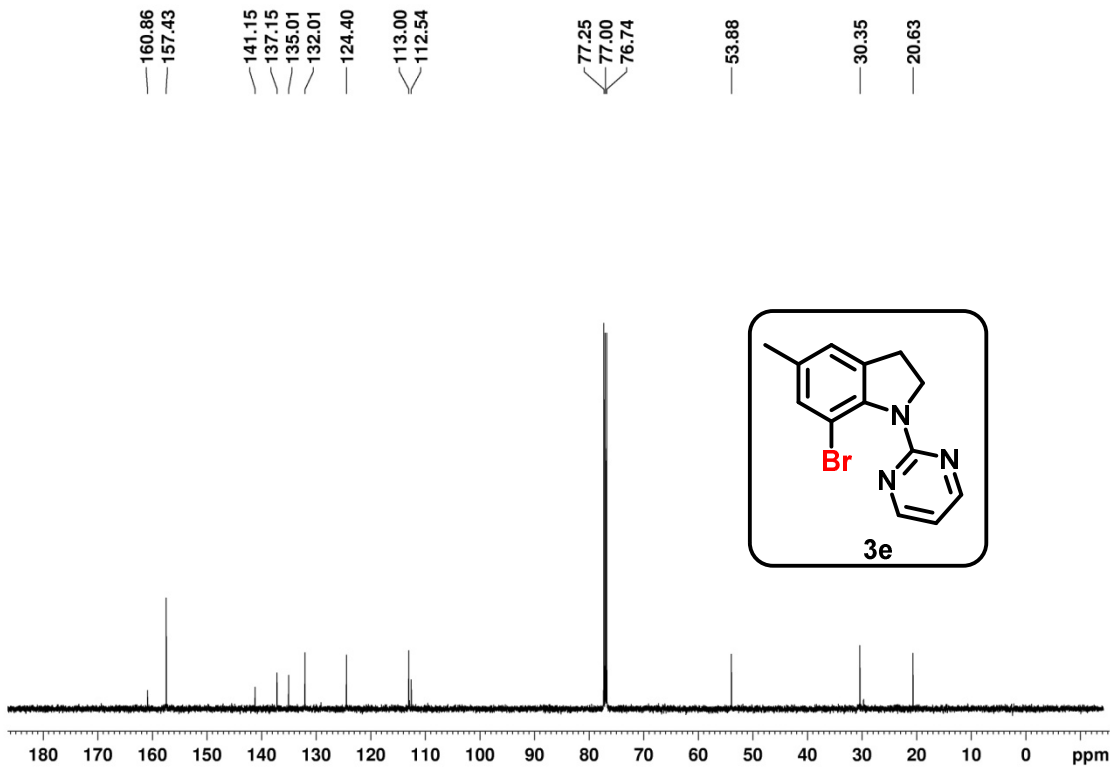
^1H NMR spectrum of **2e** (400 MHz, CDCl_3)



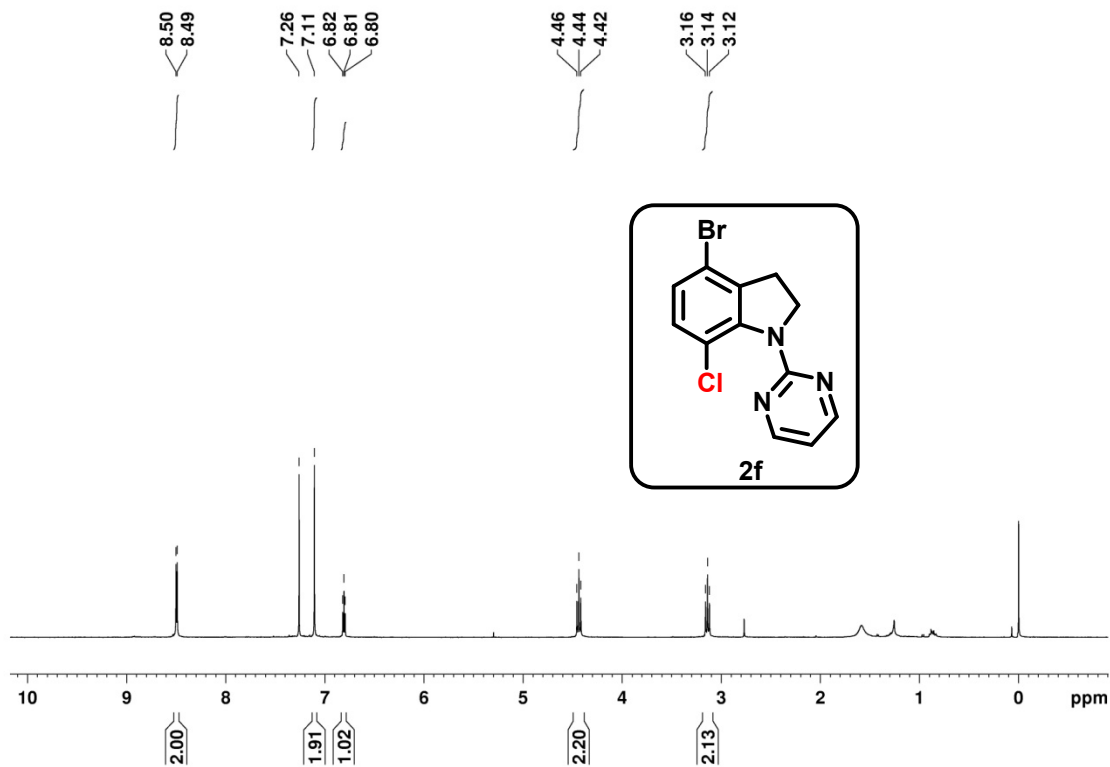
^{13}C NMR spectrum of **2e** (100 MHz, CDCl_3)



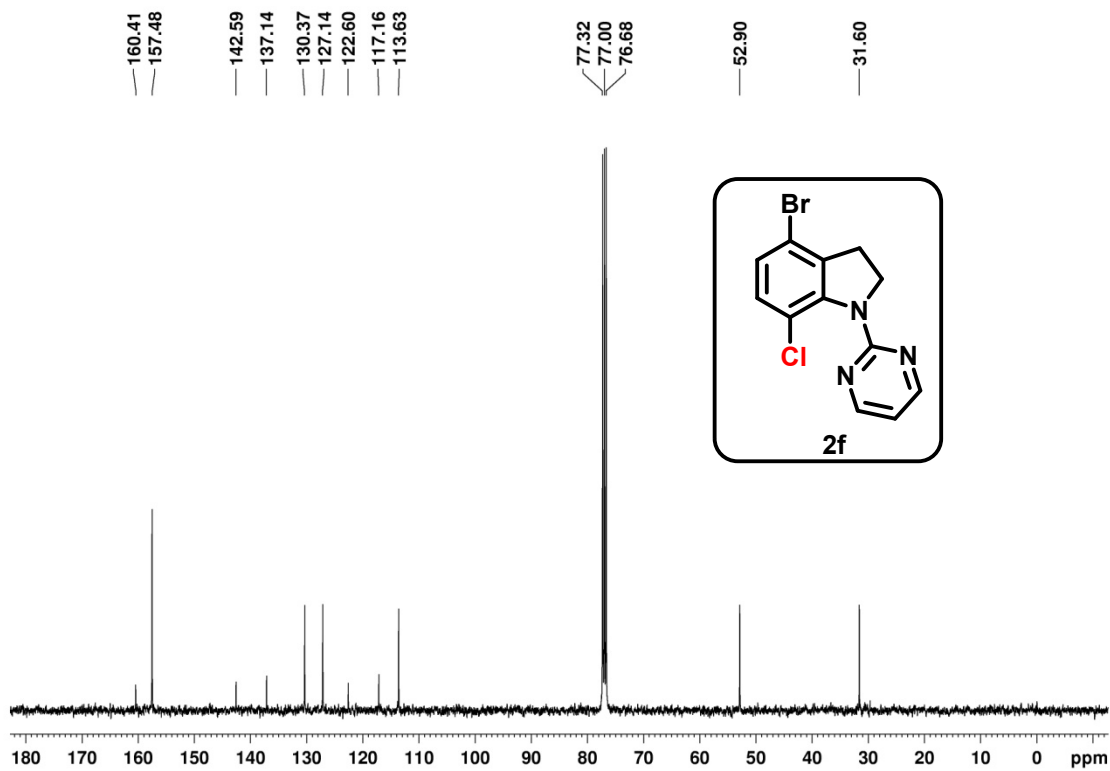
^1H NMR spectrum of **3e** (400 MHz, CDCl_3)



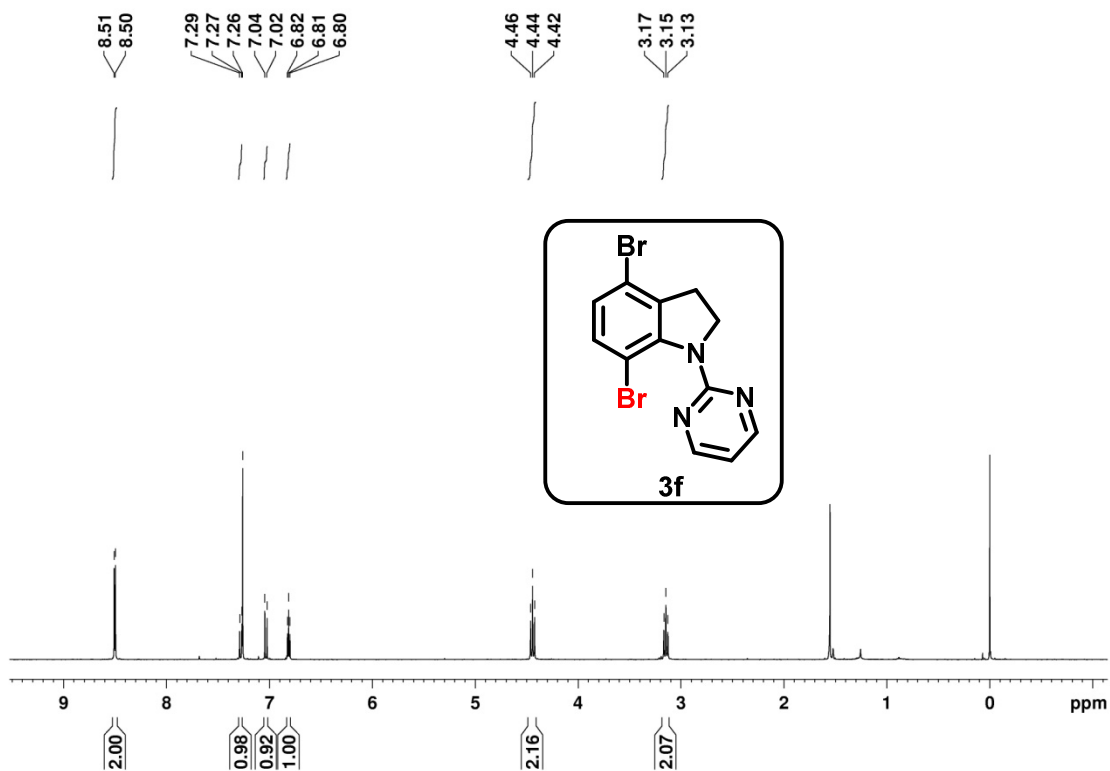
^{13}C NMR spectrum of **3e** (100 MHz, CDCl_3)



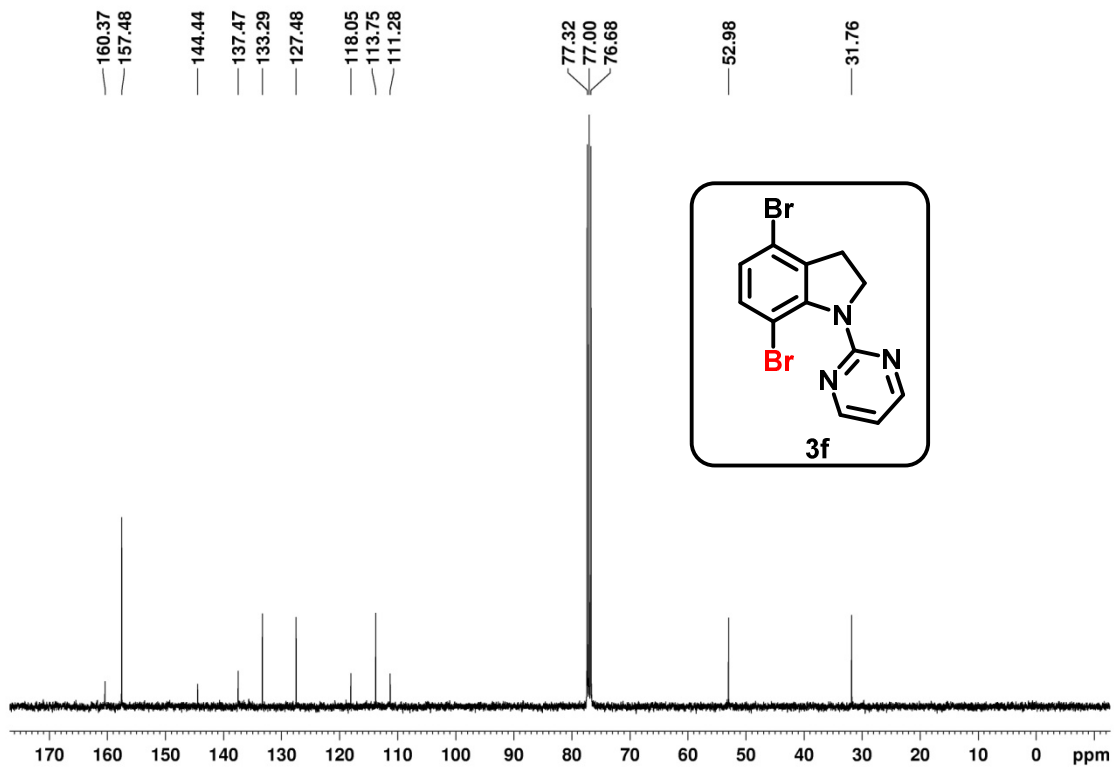
^1H NMR spectrum of **2f** (400 MHz, CDCl_3)



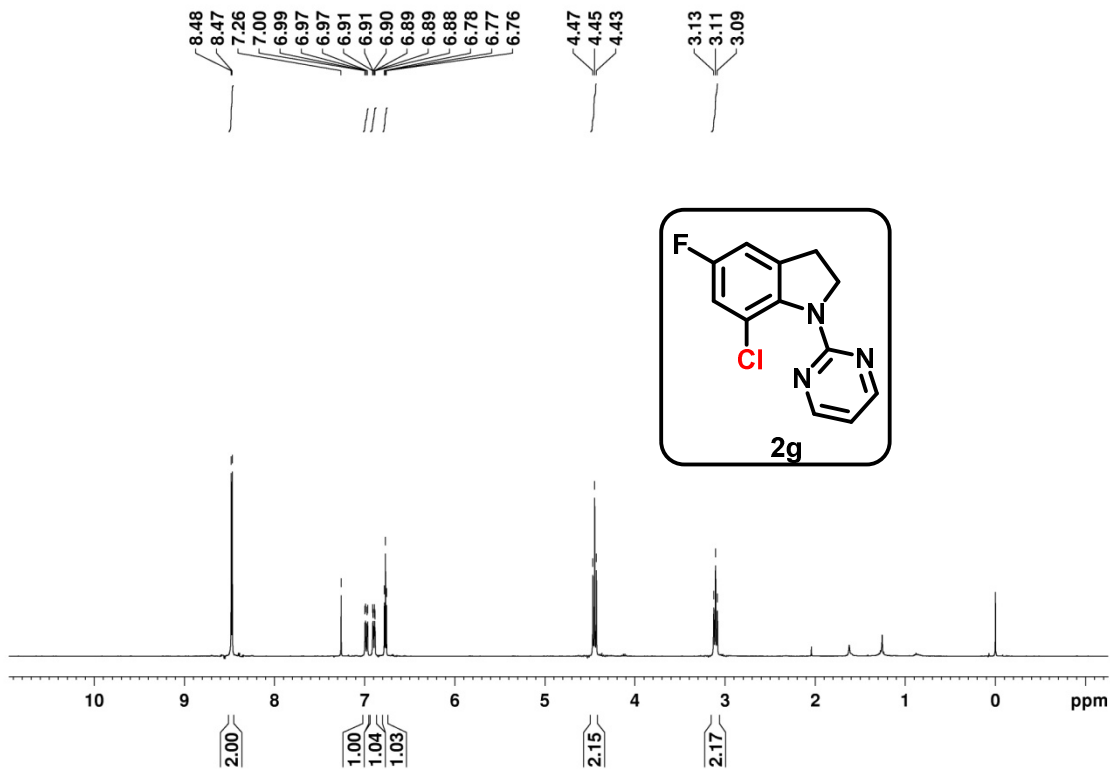
^{13}C NMR spectrum of **2f** (100 MHz, CDCl_3)



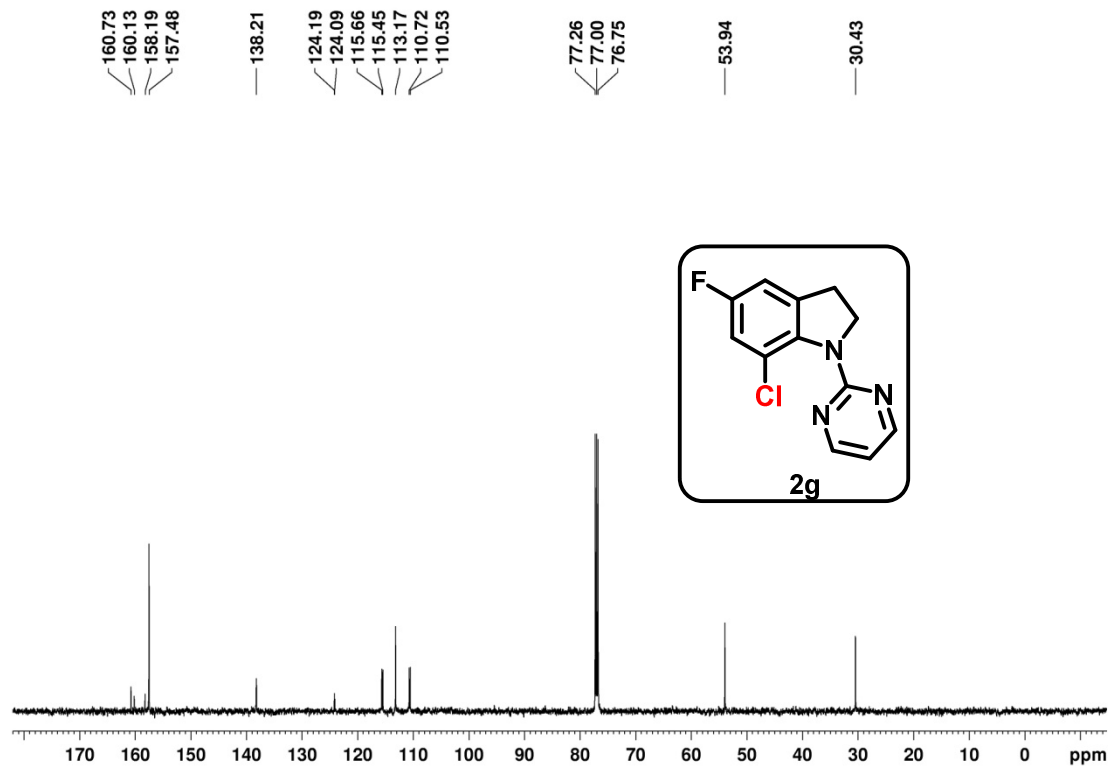
^1H NMR spectrum of **3f** (400 MHz, CDCl_3)



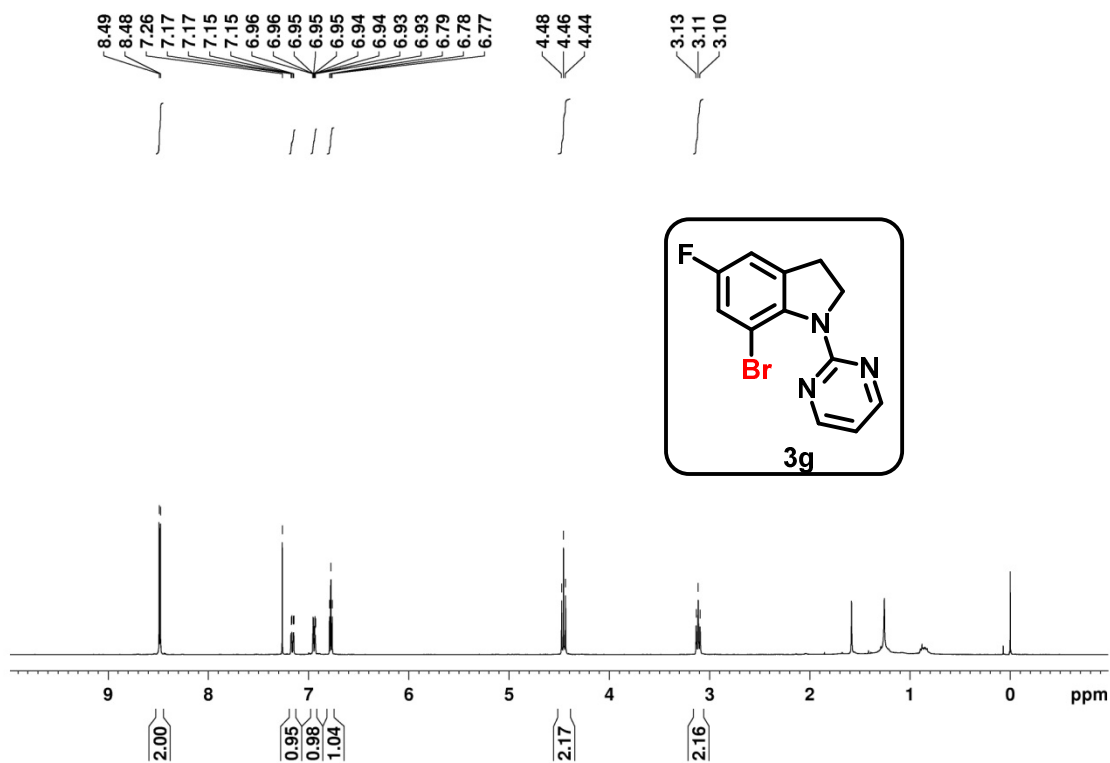
^{13}C NMR spectrum of **3f** (100 MHz, CDCl_3)



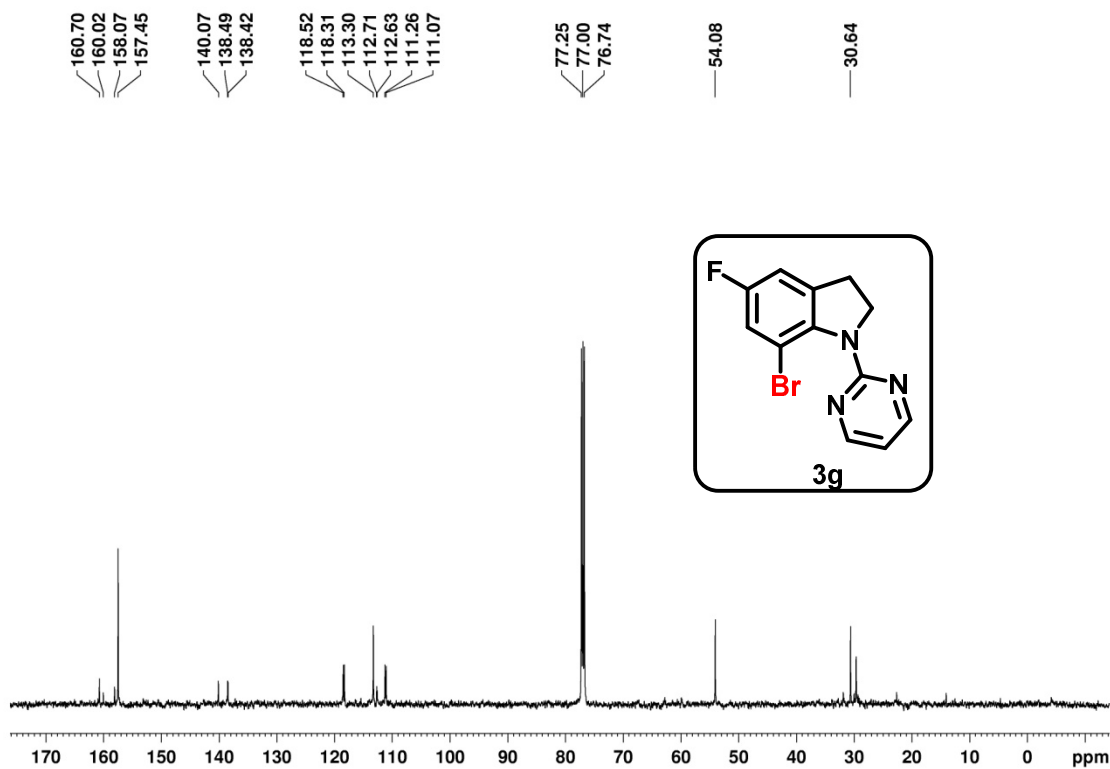
^1H NMR spectrum of **2g** (400 MHz, CDCl_3)



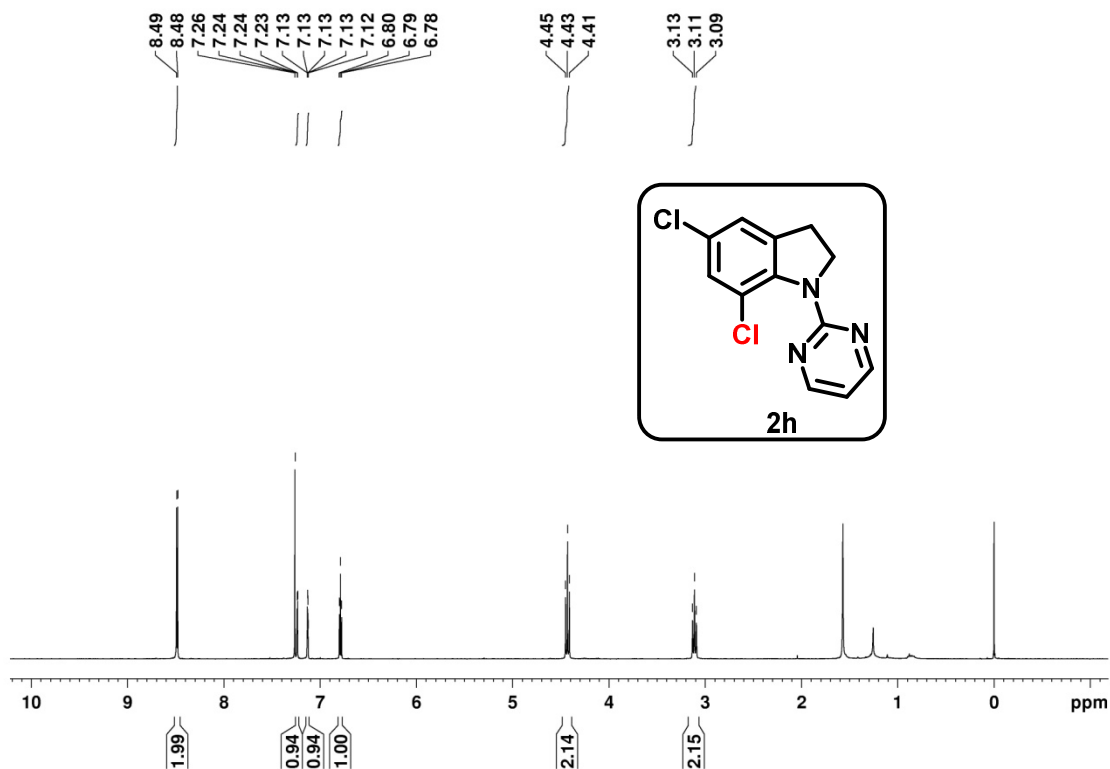
^{13}C NMR spectrum of **2g** (100 MHz, CDCl_3)



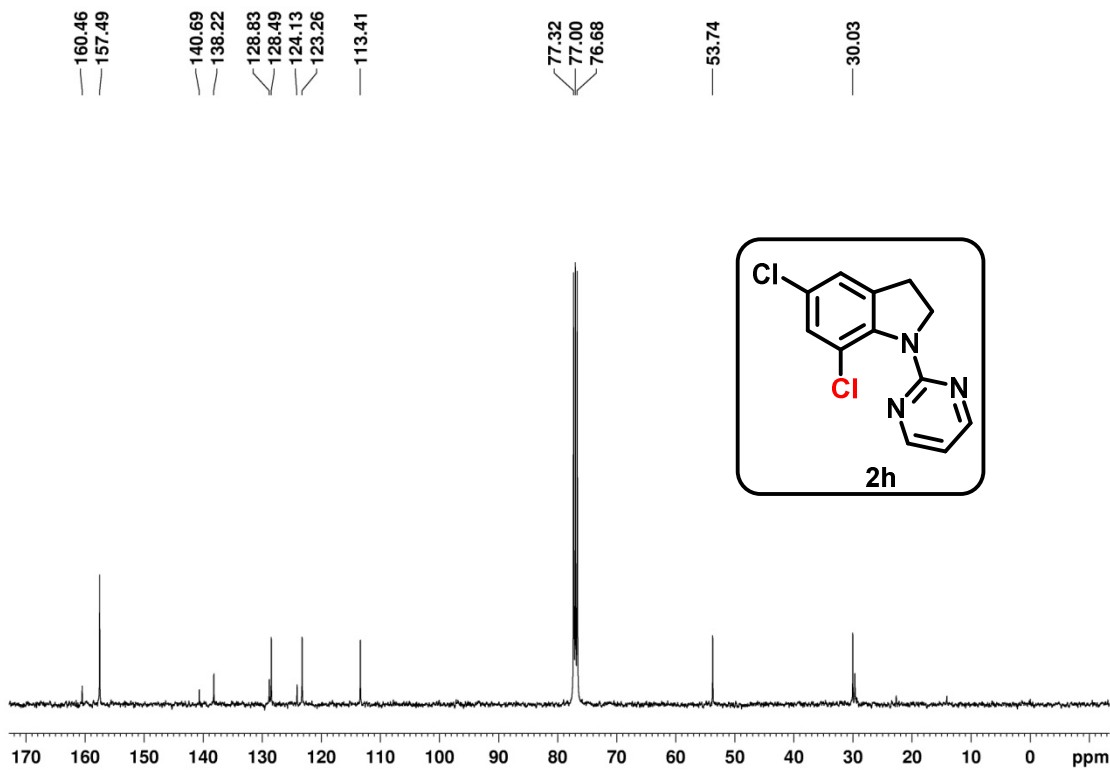
¹H NMR spectrum of **3g** (400 MHz, CDCl₃)



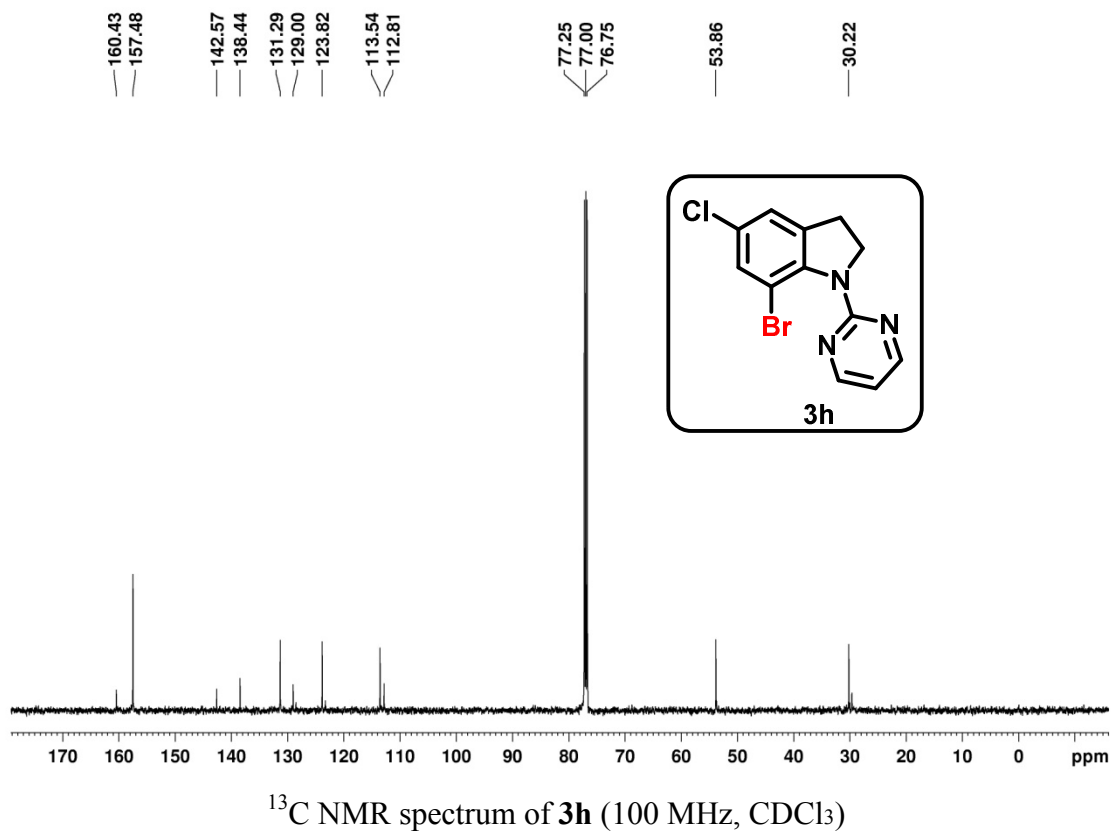
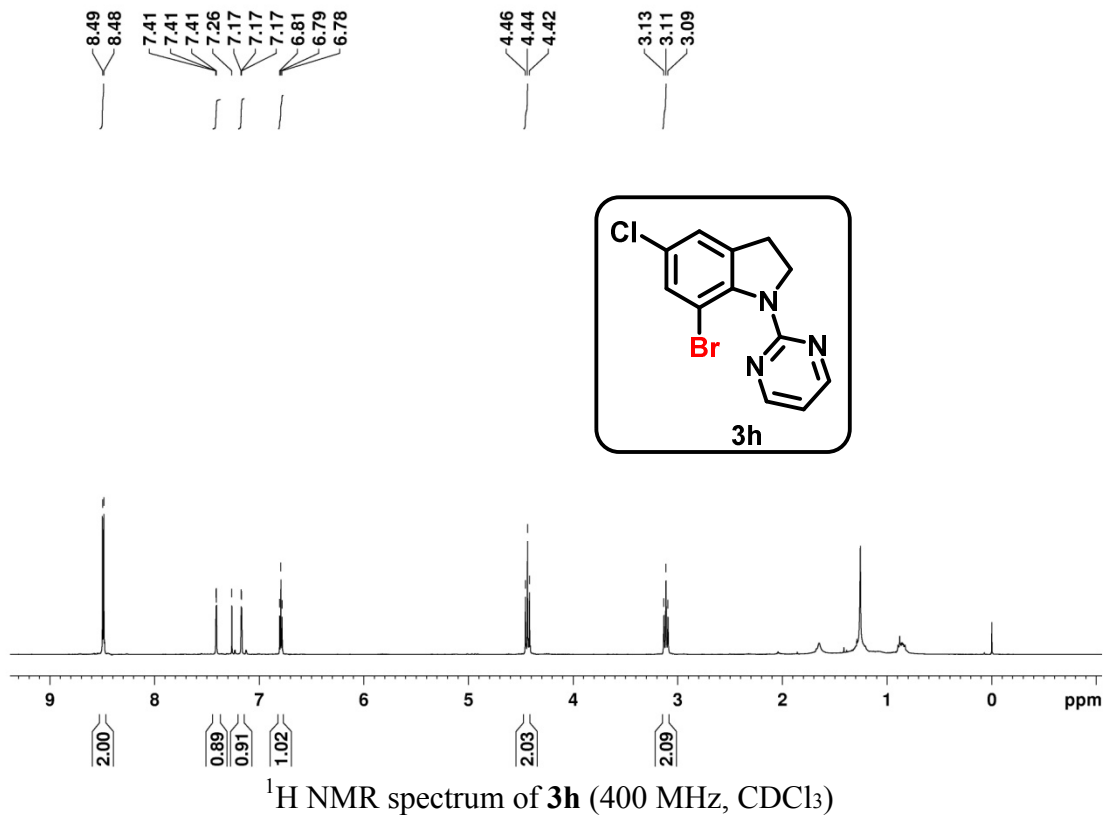
¹³C NMR spectrum of **3g** (100 MHz, CDCl₃)

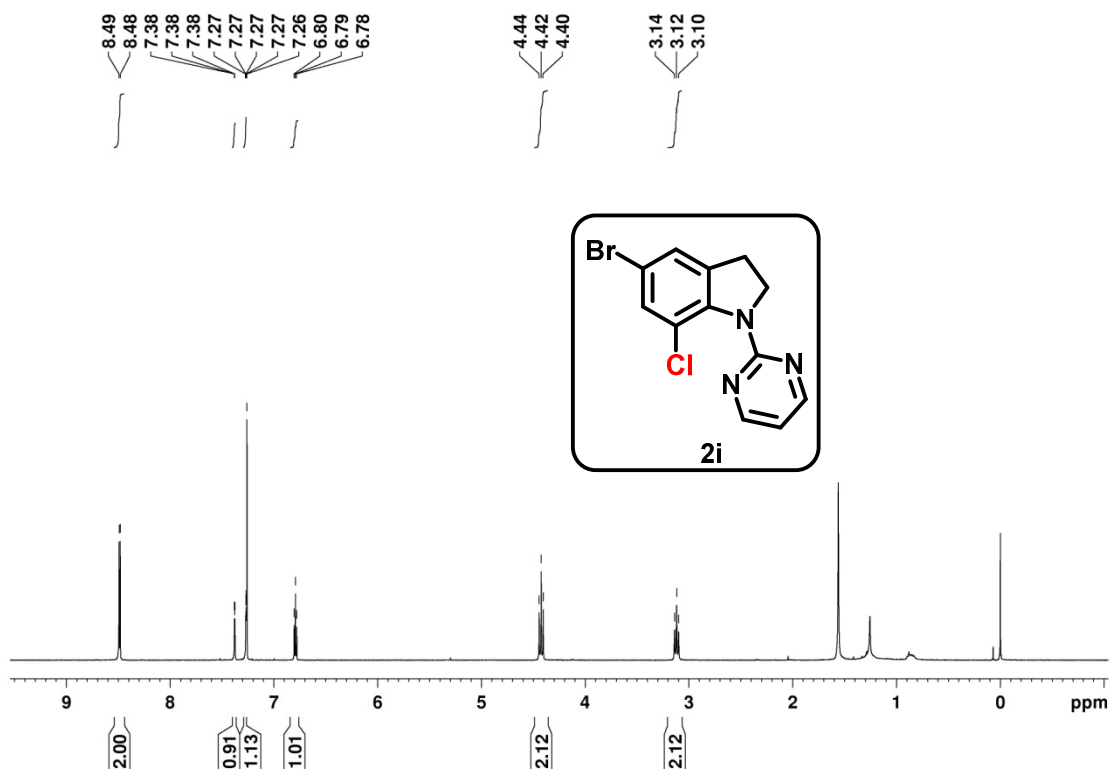


¹H NMR spectrum of **2h** (400 MHz, CDCl₃)

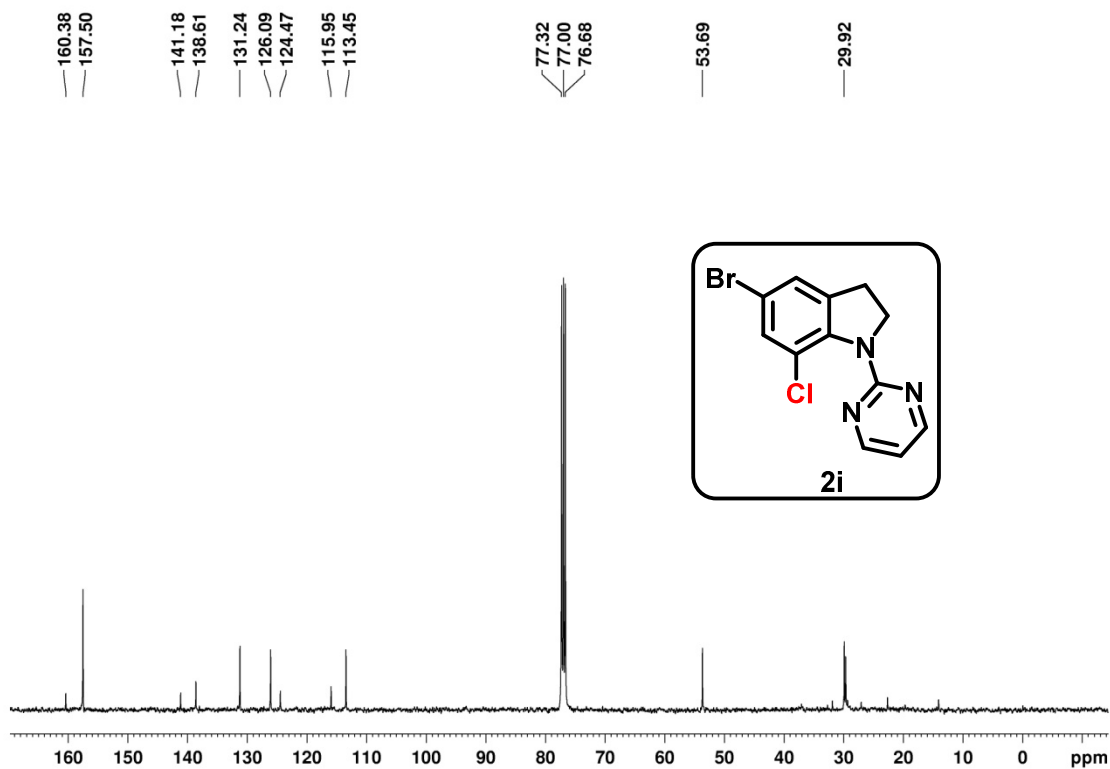


¹³C NMR spectrum of **2h** (100 MHz, CDCl₃)

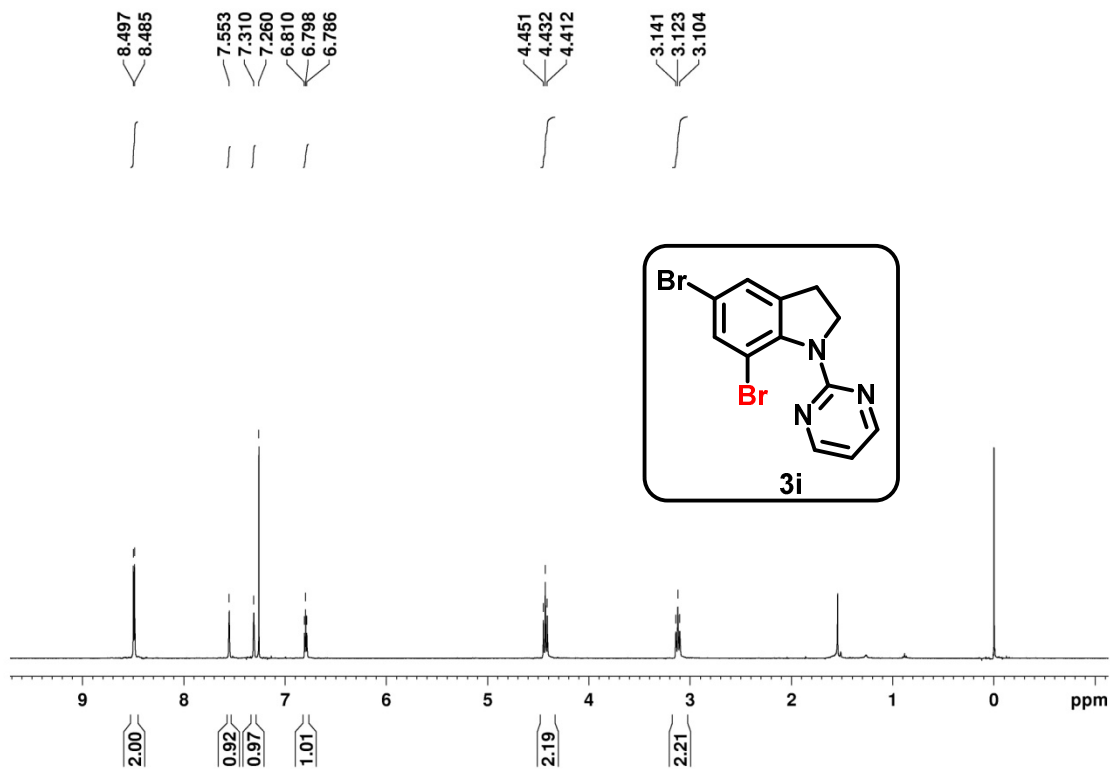




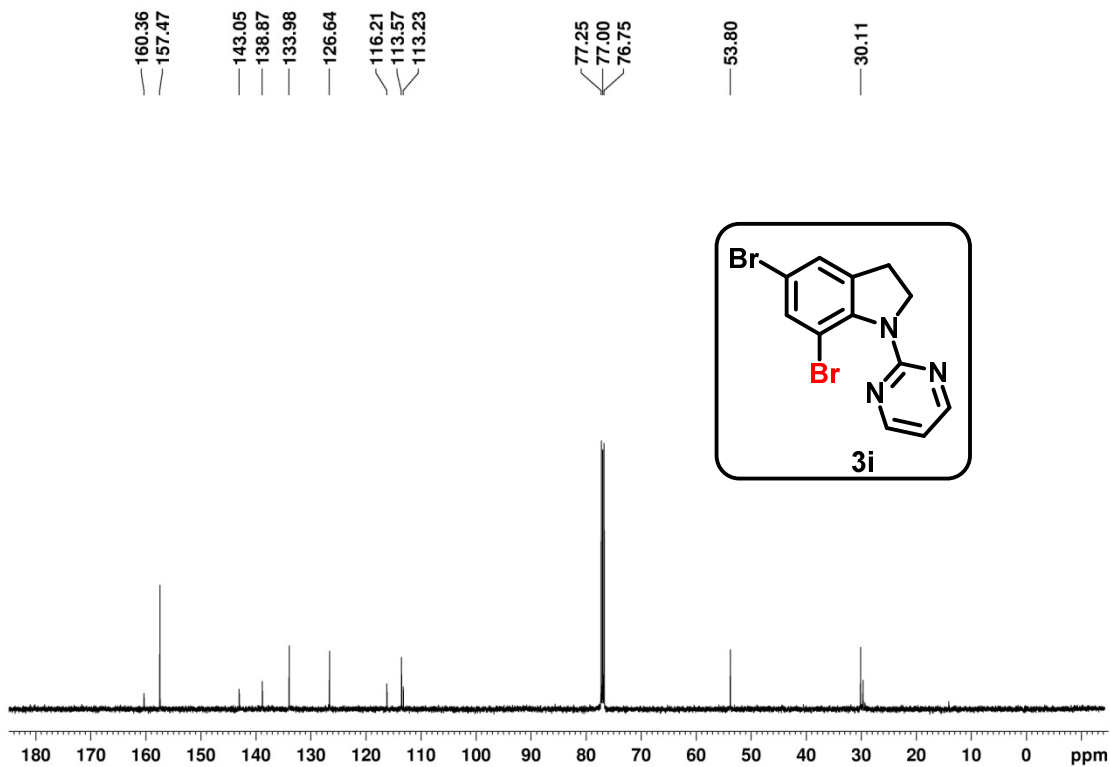
^1H NMR spectrum of **2i** (400 MHz, CDCl_3)



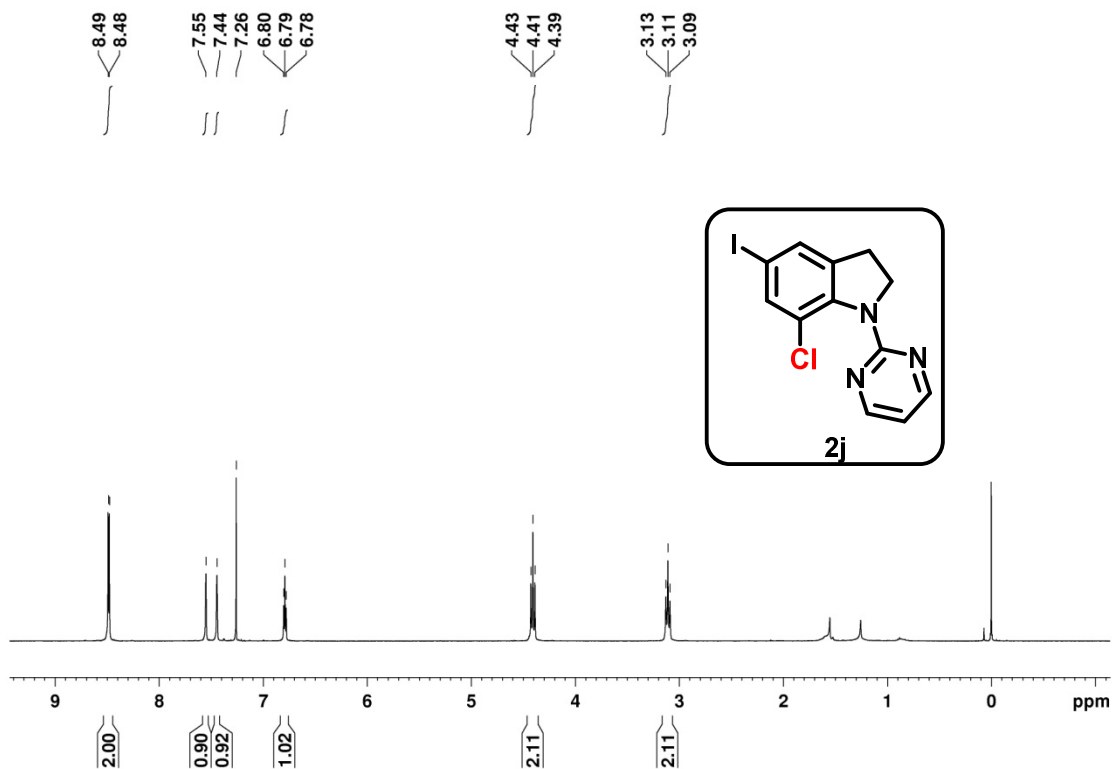
^{13}C NMR spectrum of **2i** (100 MHz, CDCl_3)



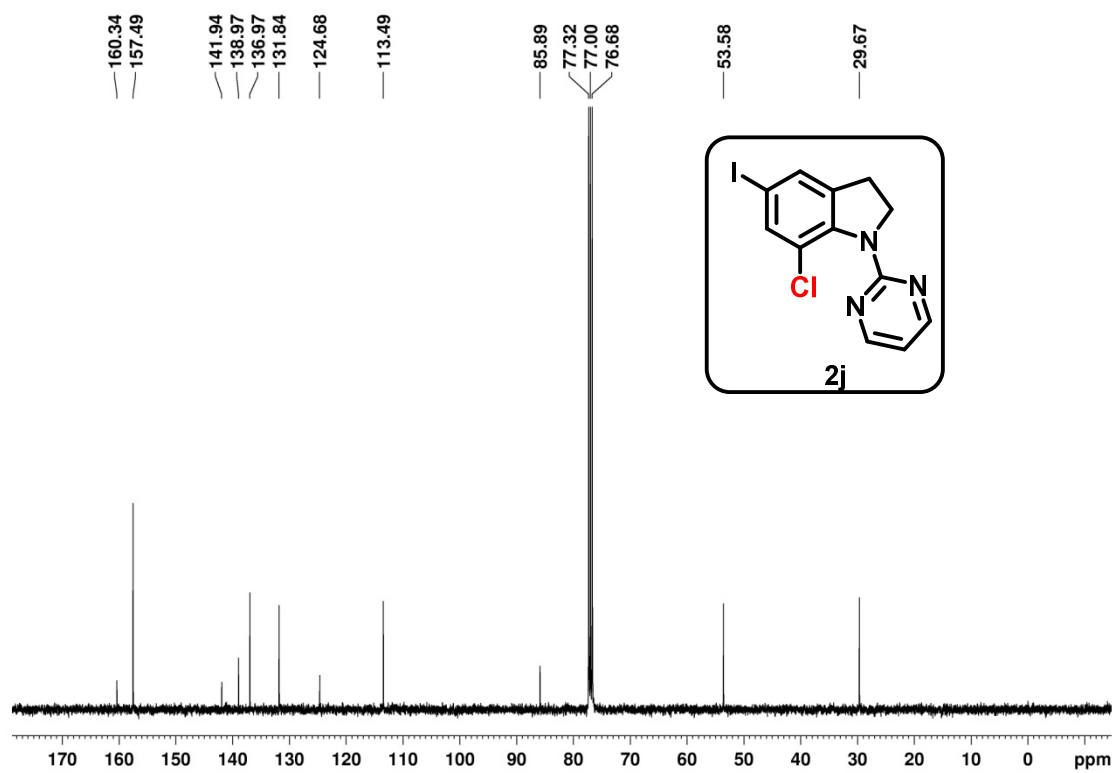
^1H NMR spectrum of **3i** (400 MHz, CDCl_3)



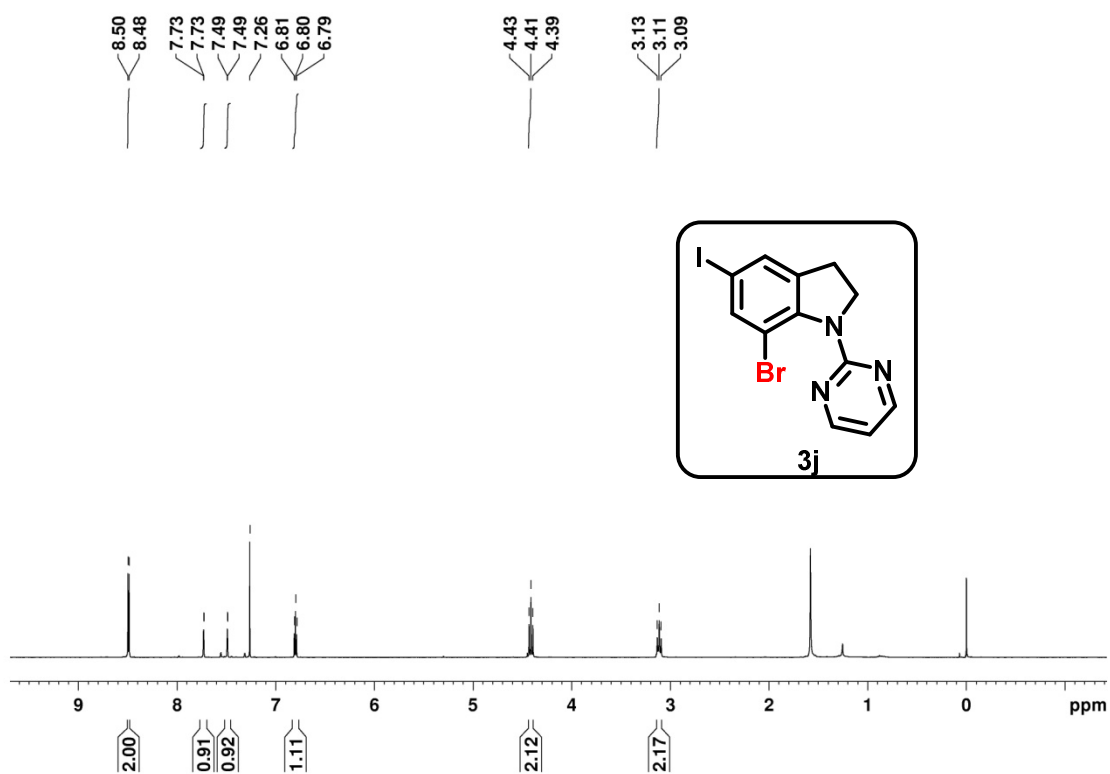
^{13}C NMR spectrum of **3i** (100 MHz, CDCl_3)



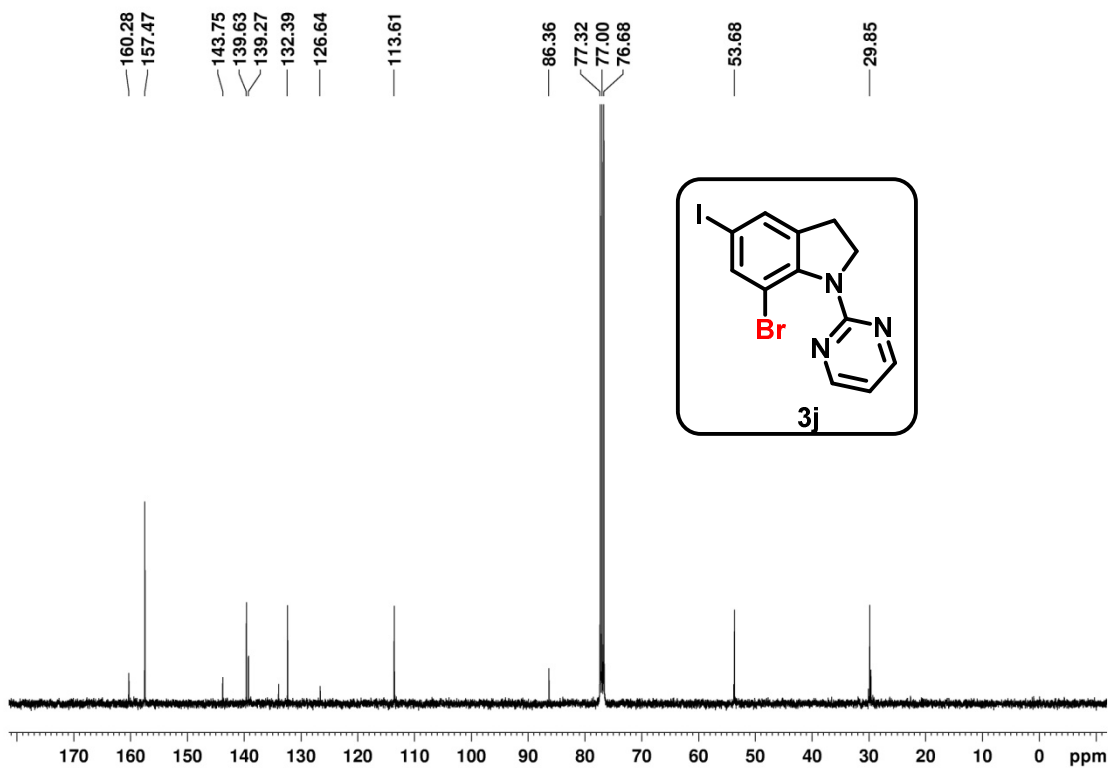
^1H NMR spectrum of **2j** (400 MHz, CDCl_3)



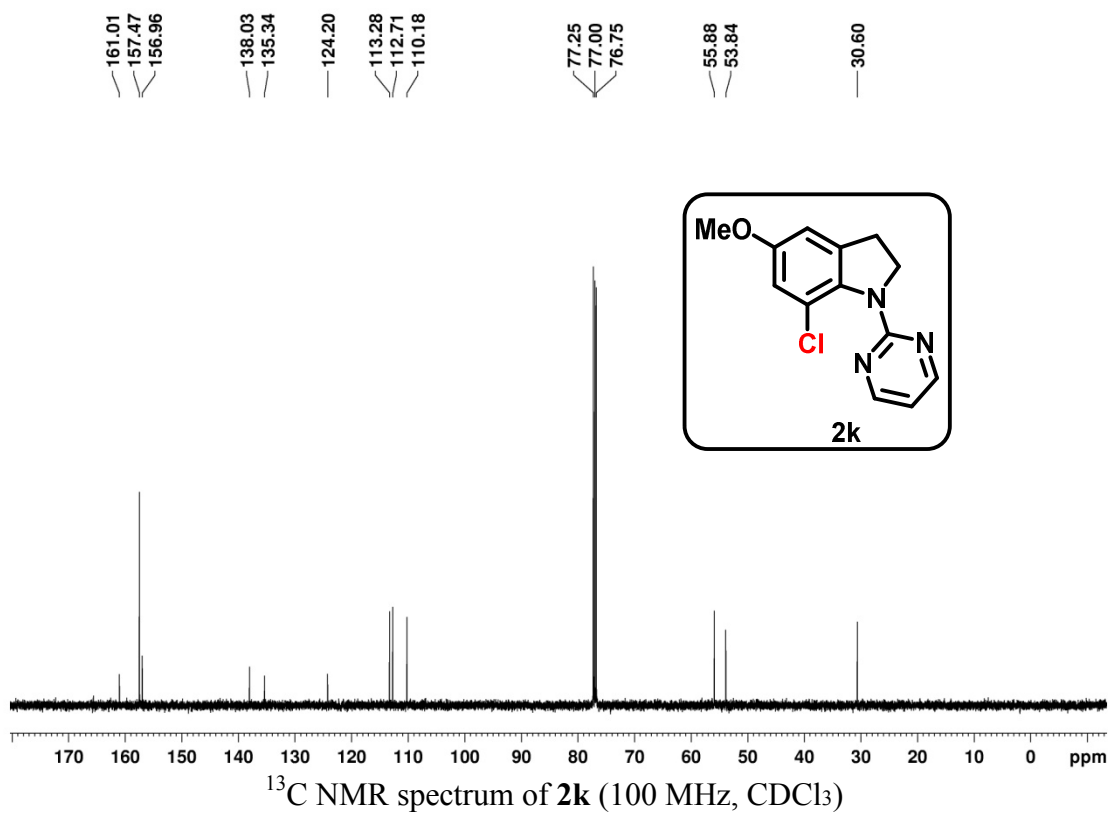
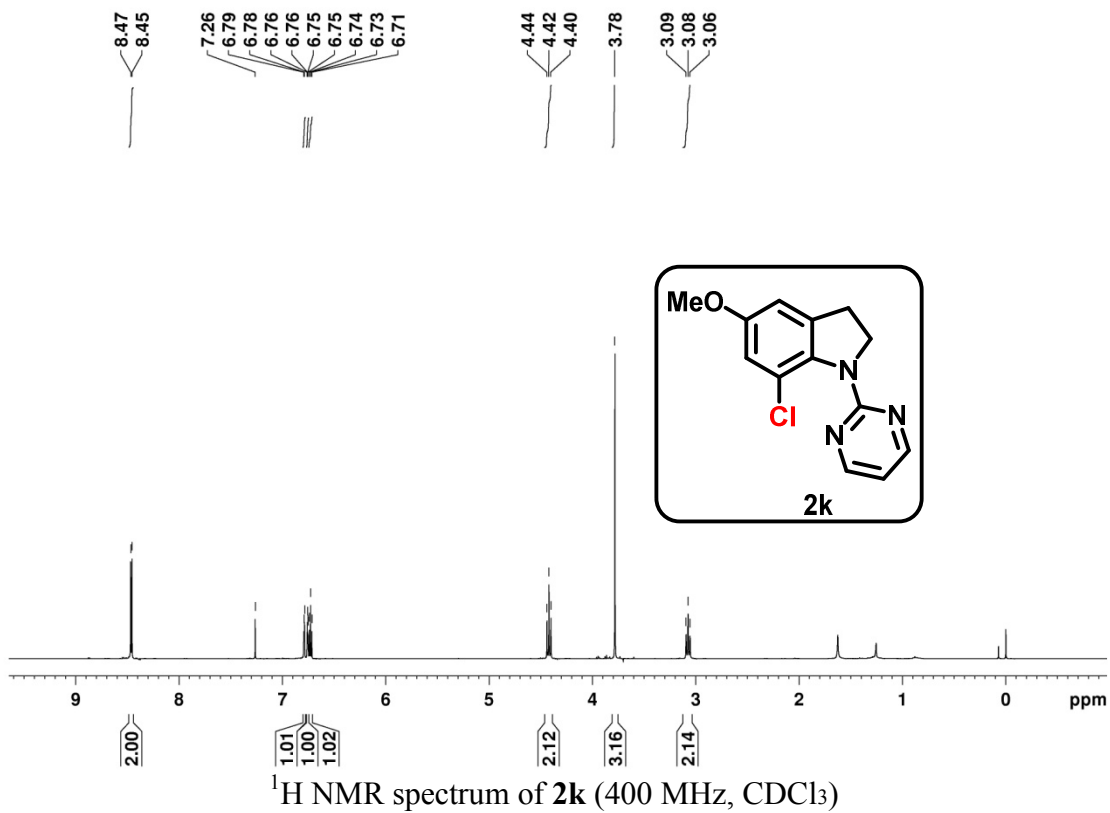
^{13}C NMR spectrum of **2j** (100 MHz, CDCl_3)

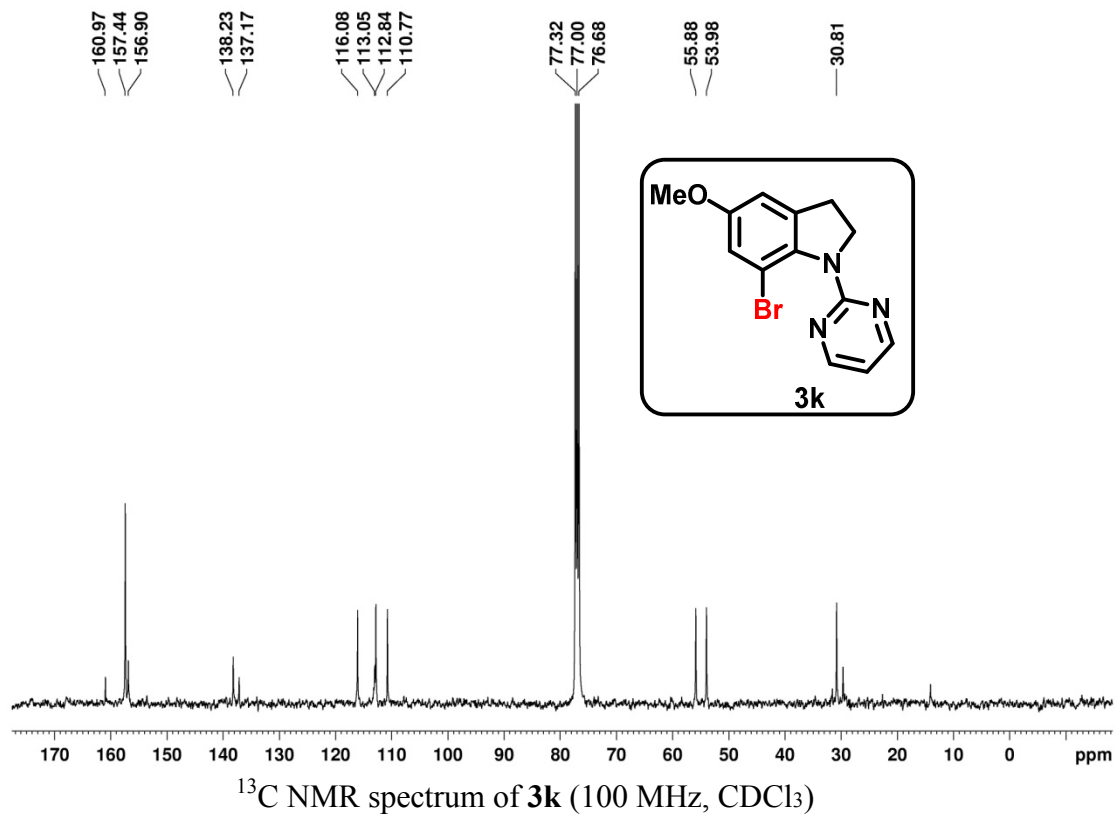
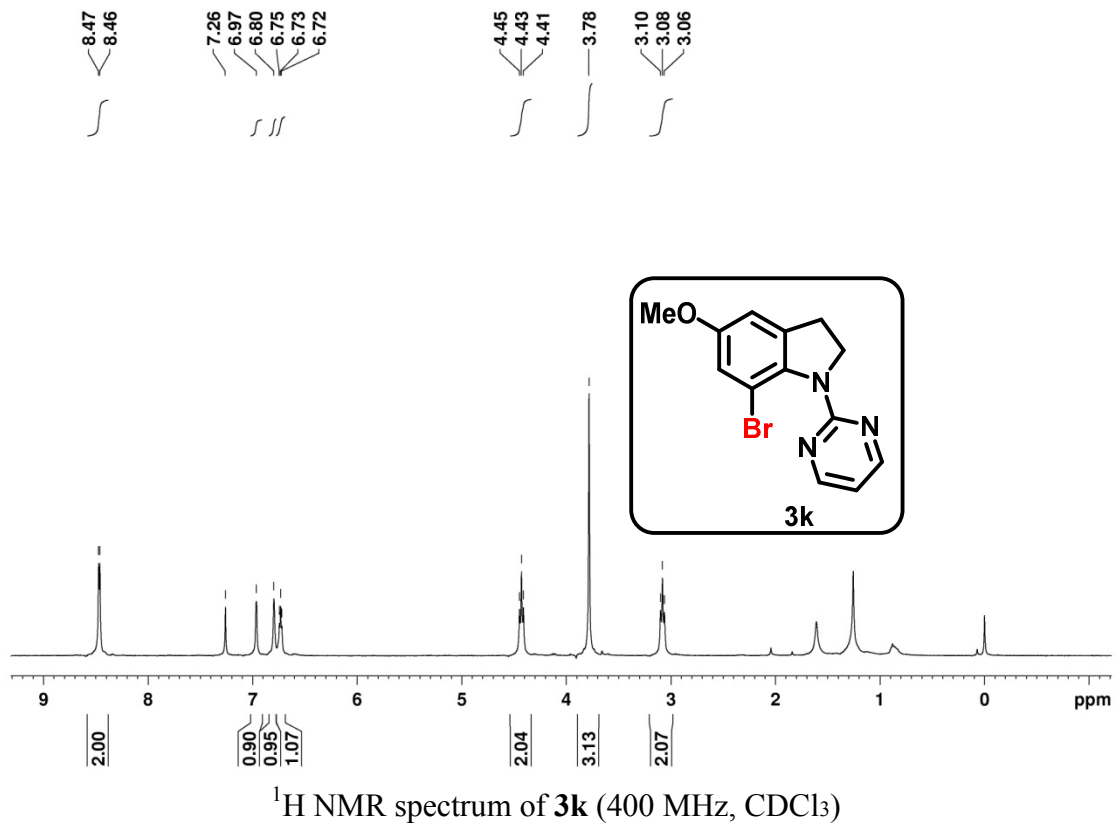


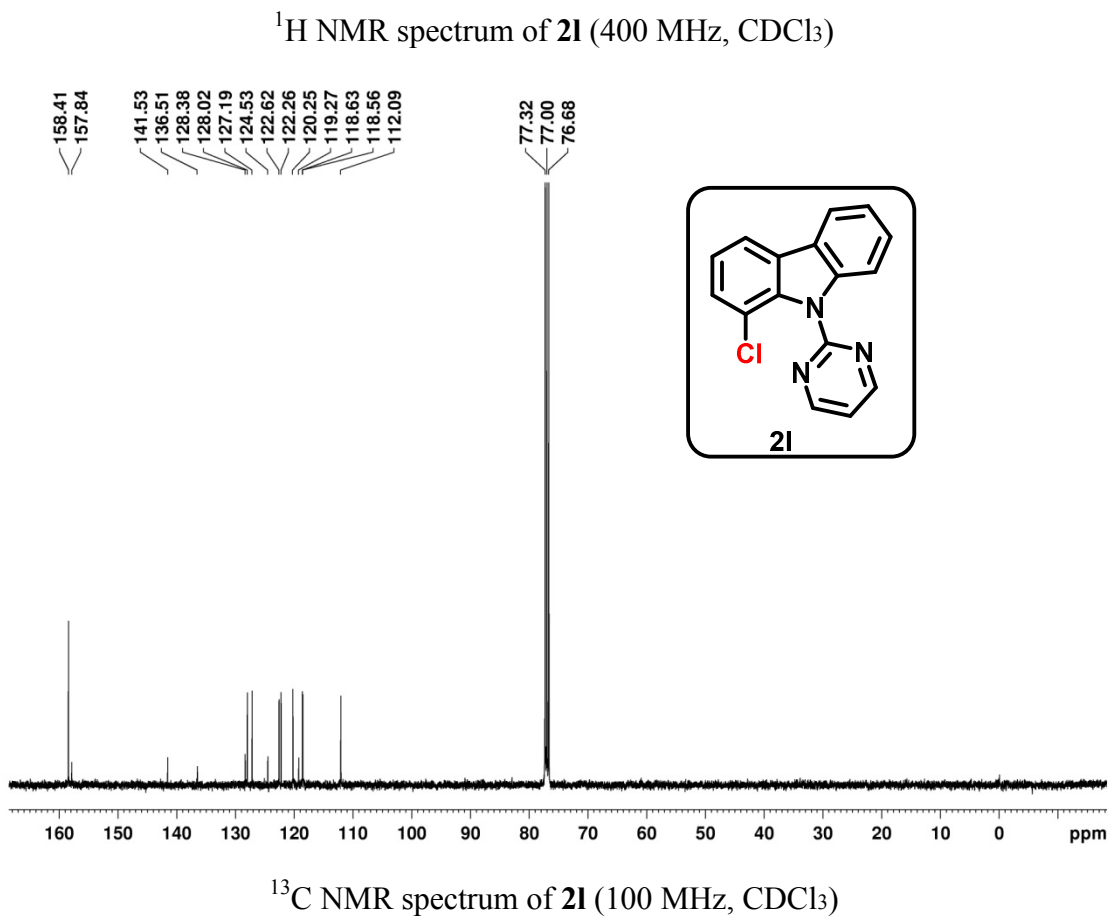
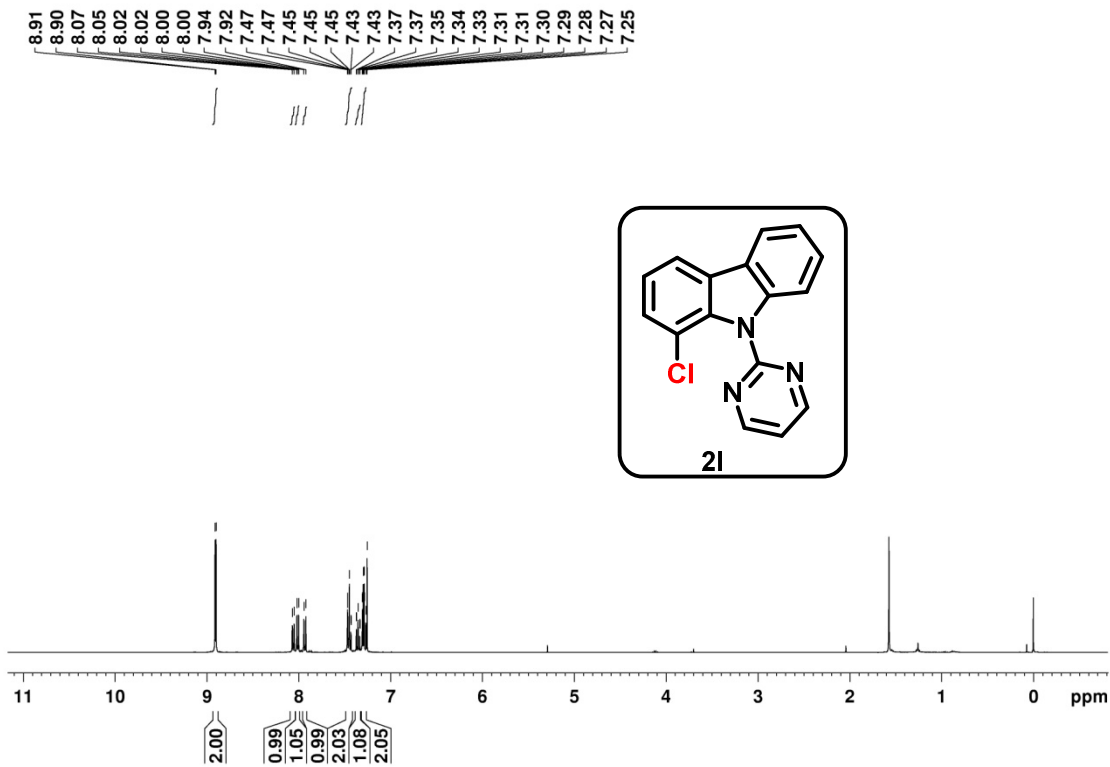
¹H NMR spectrum of **3j** (400 MHz, CDCl₃)

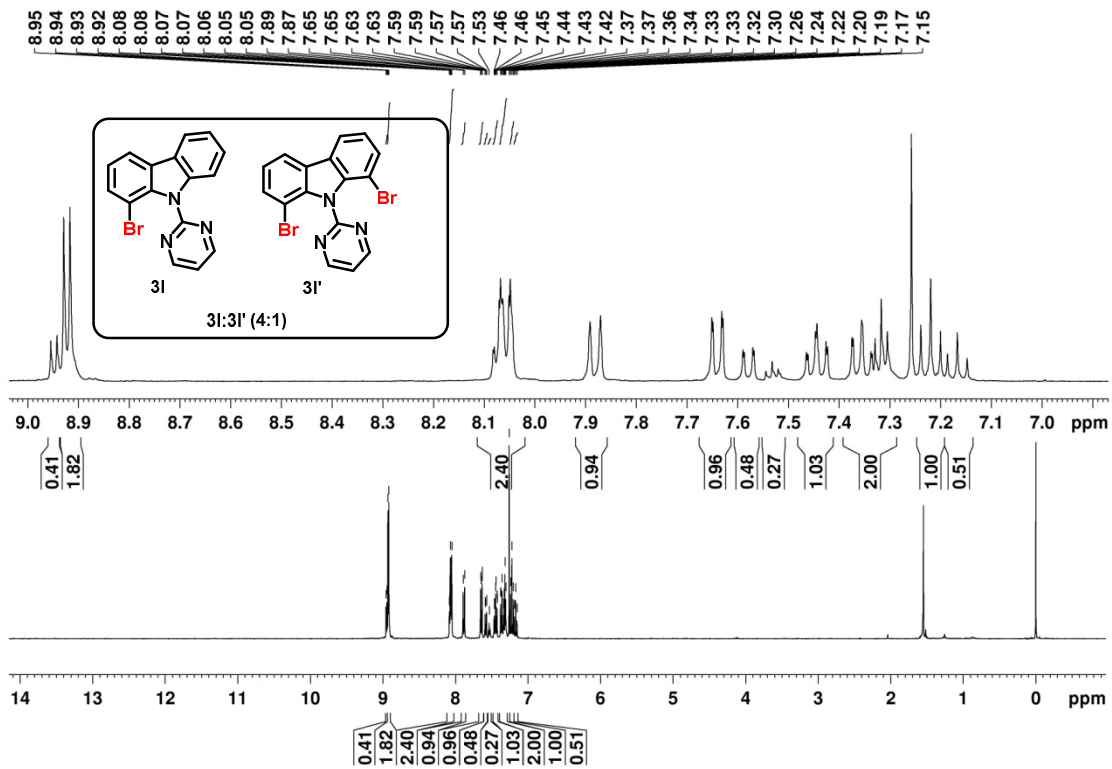


¹³C NMR spectrum of **3j** (100 MHz, CDCl₃)

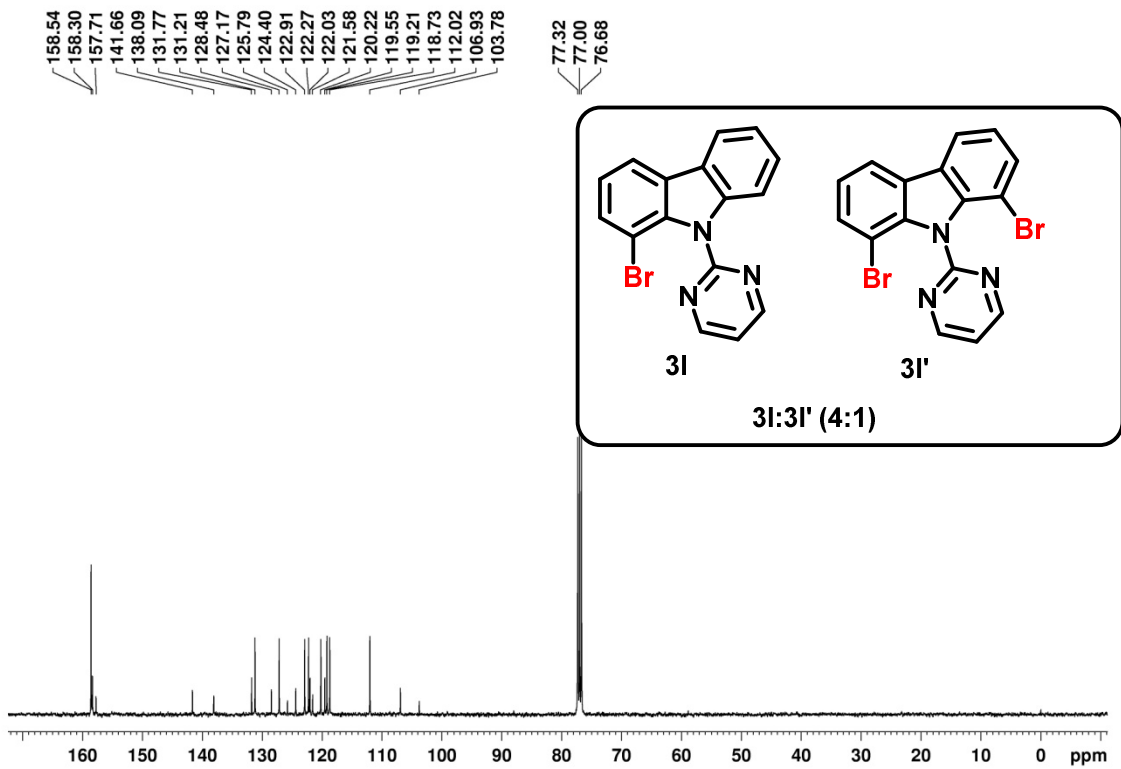




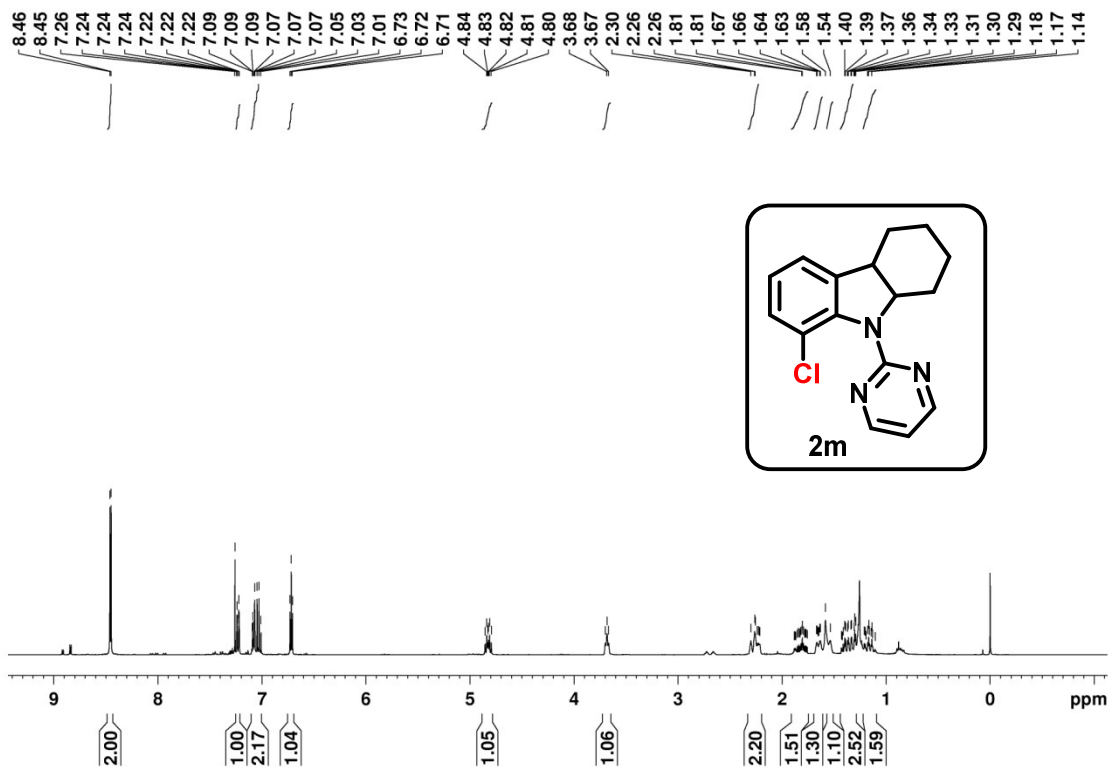




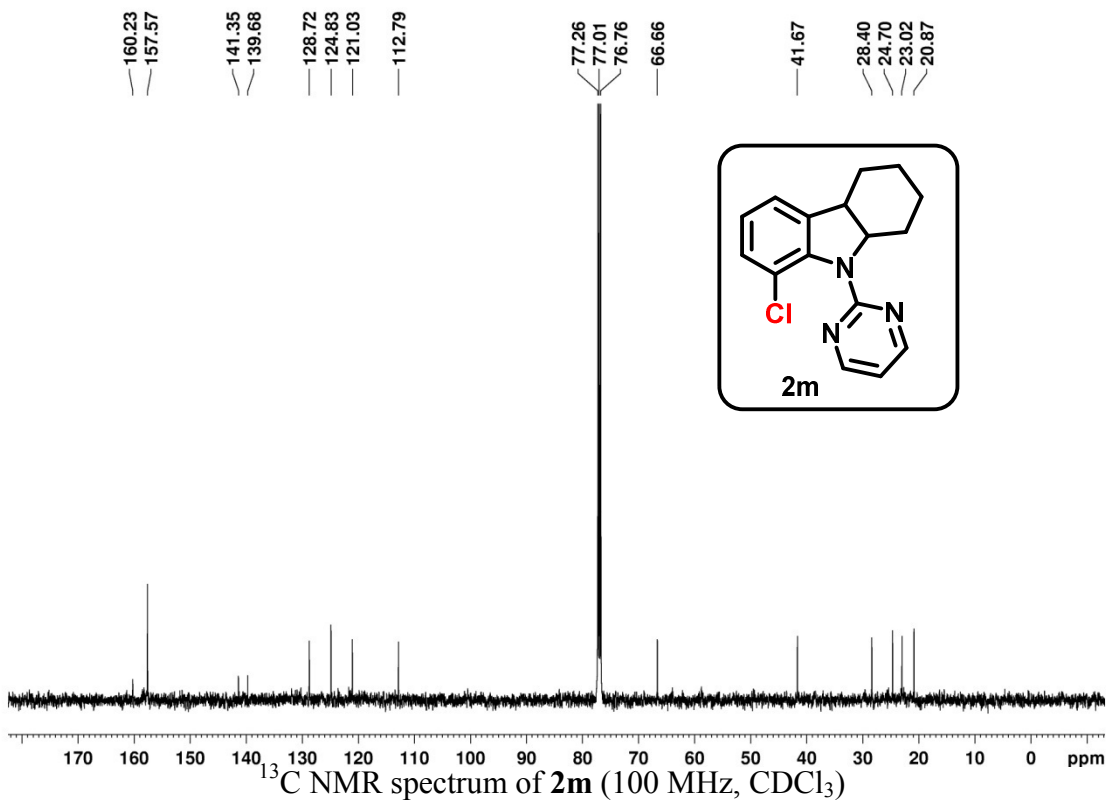
^1H NMR spectrum of **3I** (400 MHz, CDCl_3)



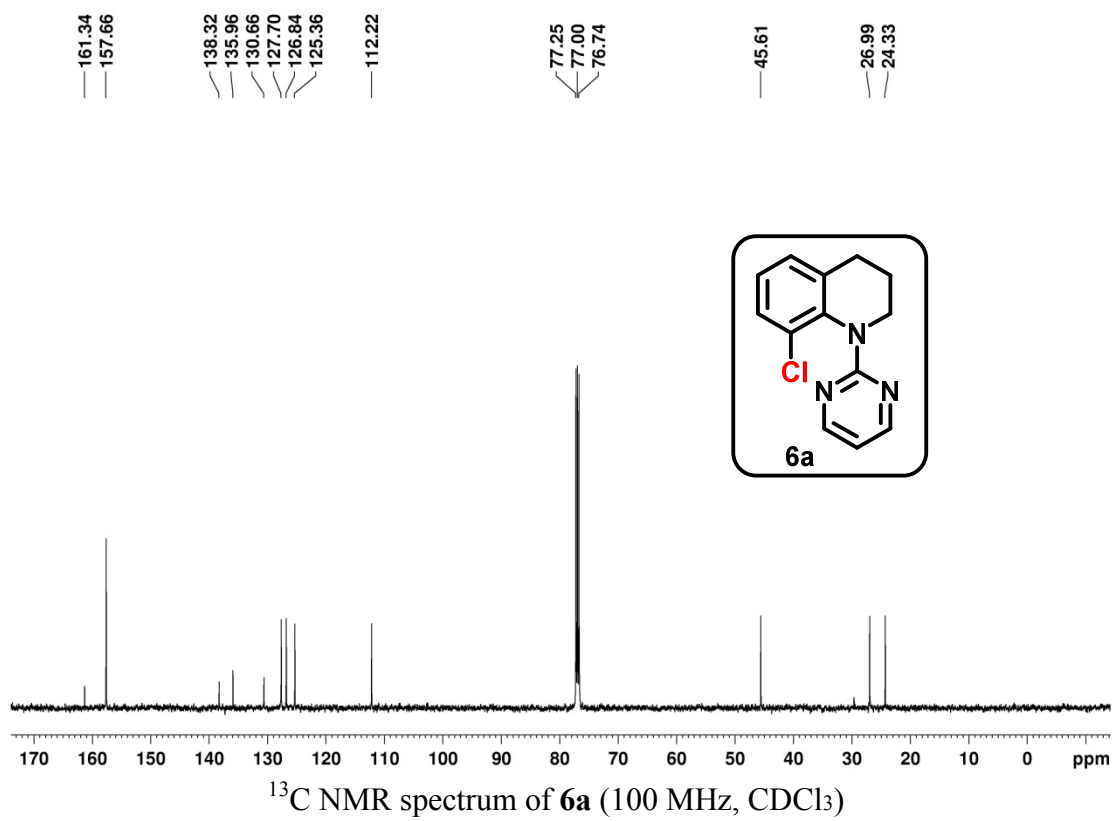
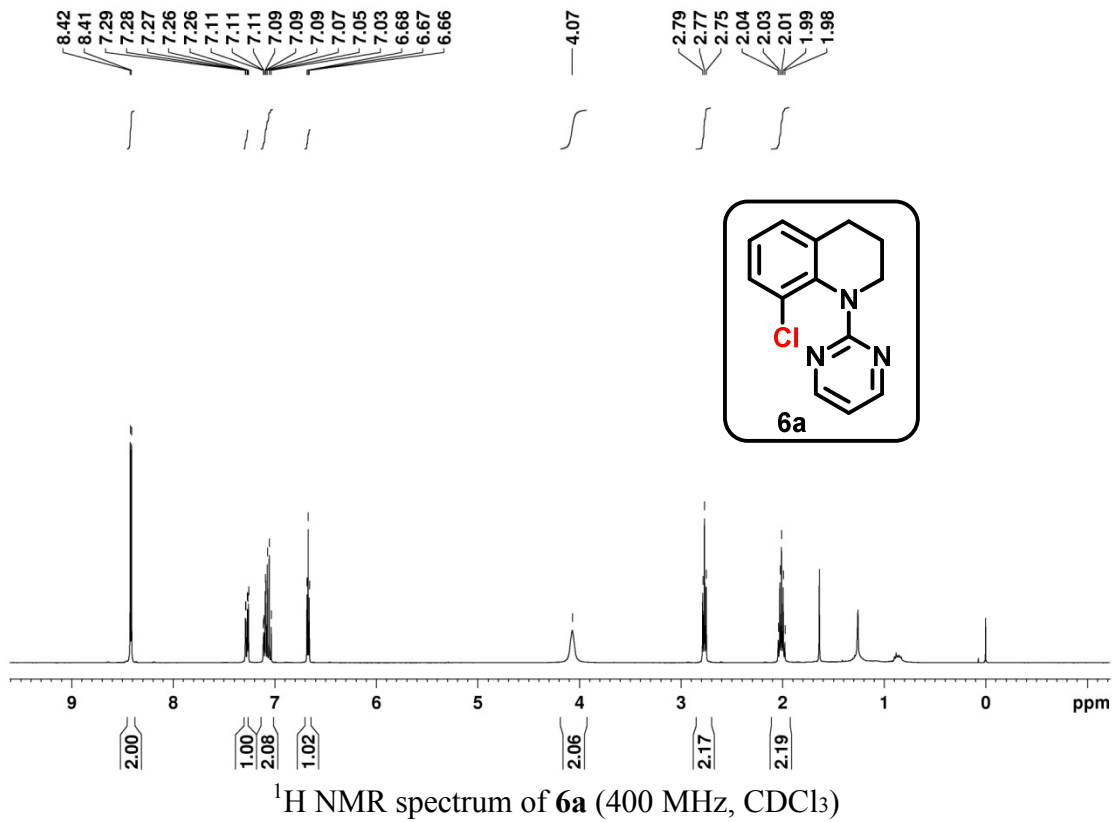
^{13}C NMR spectrum of **3I** (100 MHz, CDCl_3)

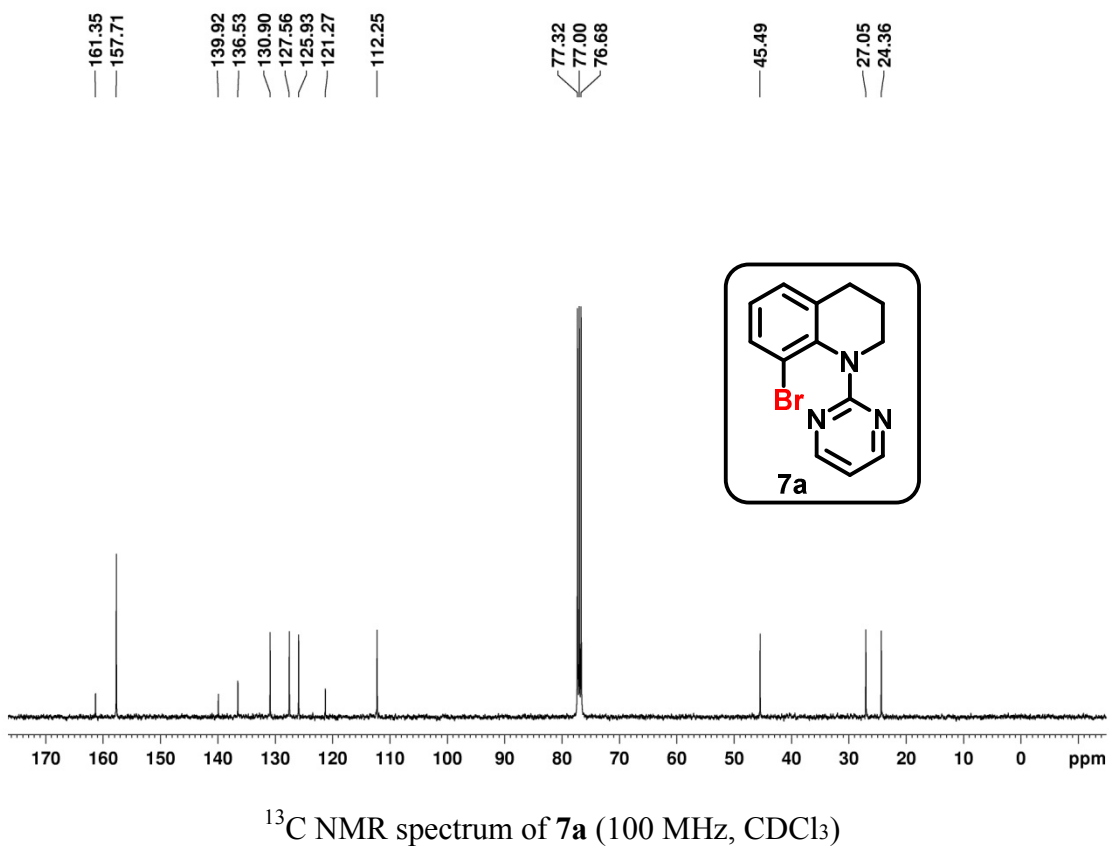
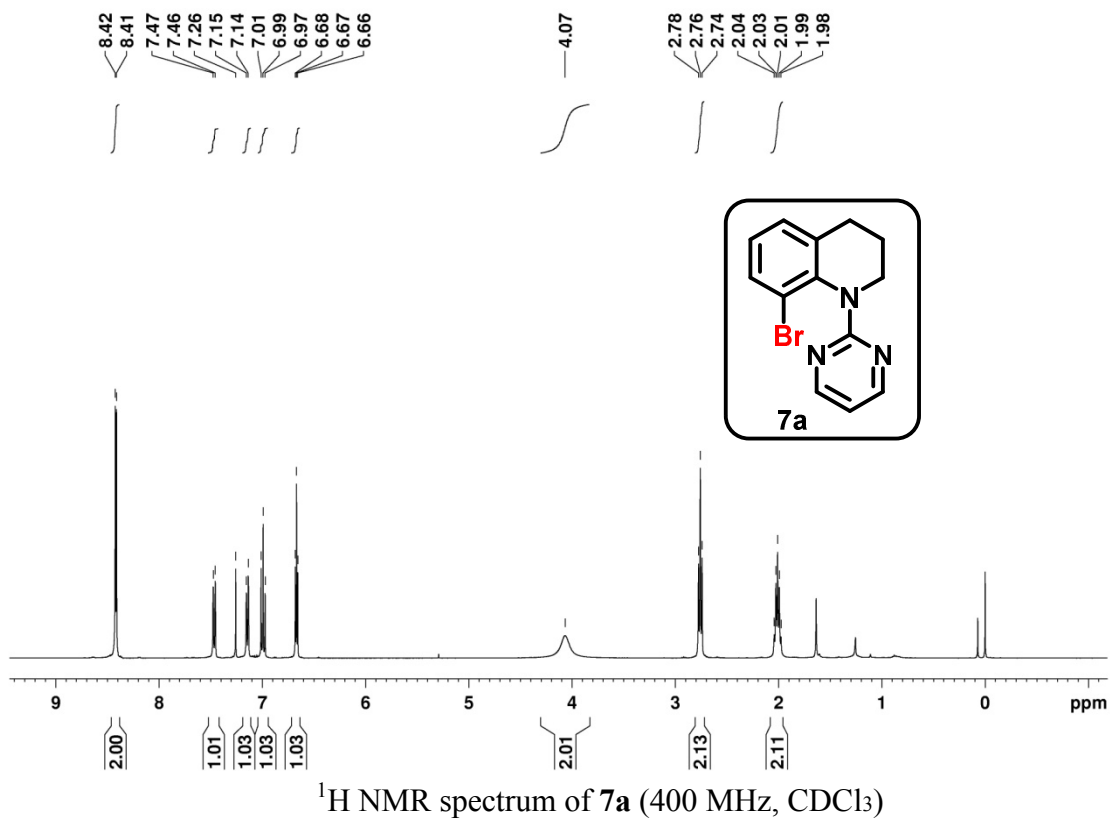


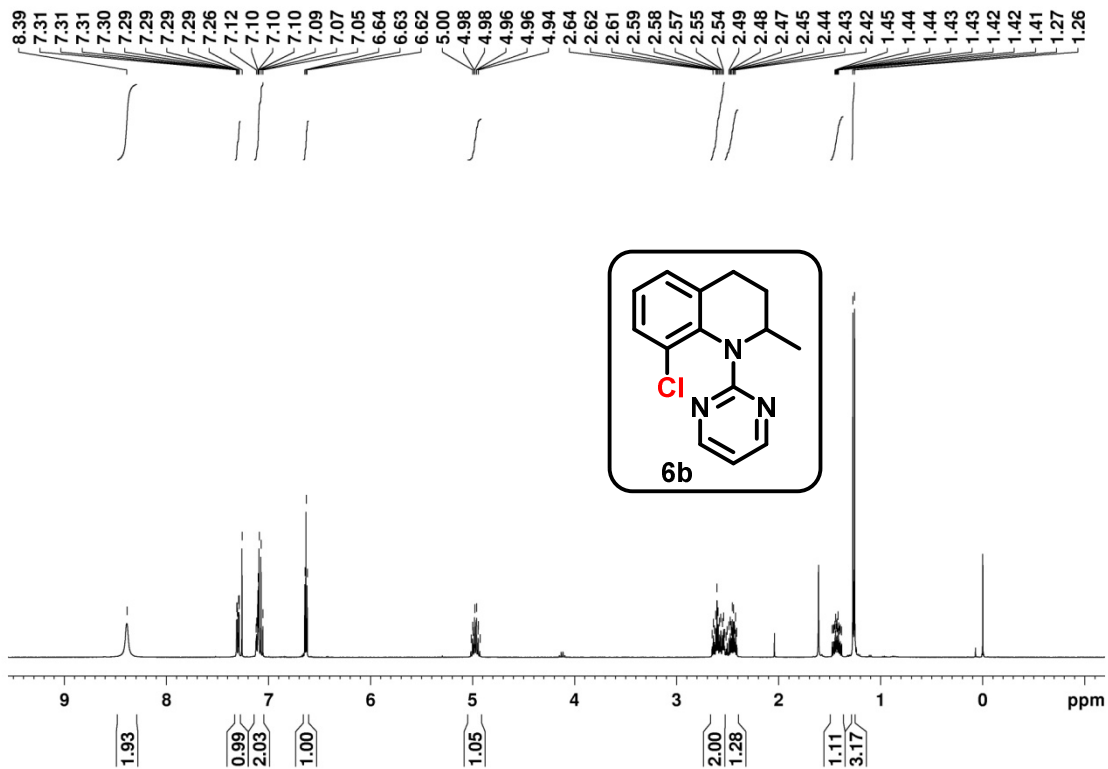
^1H NMR spectrum of **2m** (400 MHz, CDCl_3)



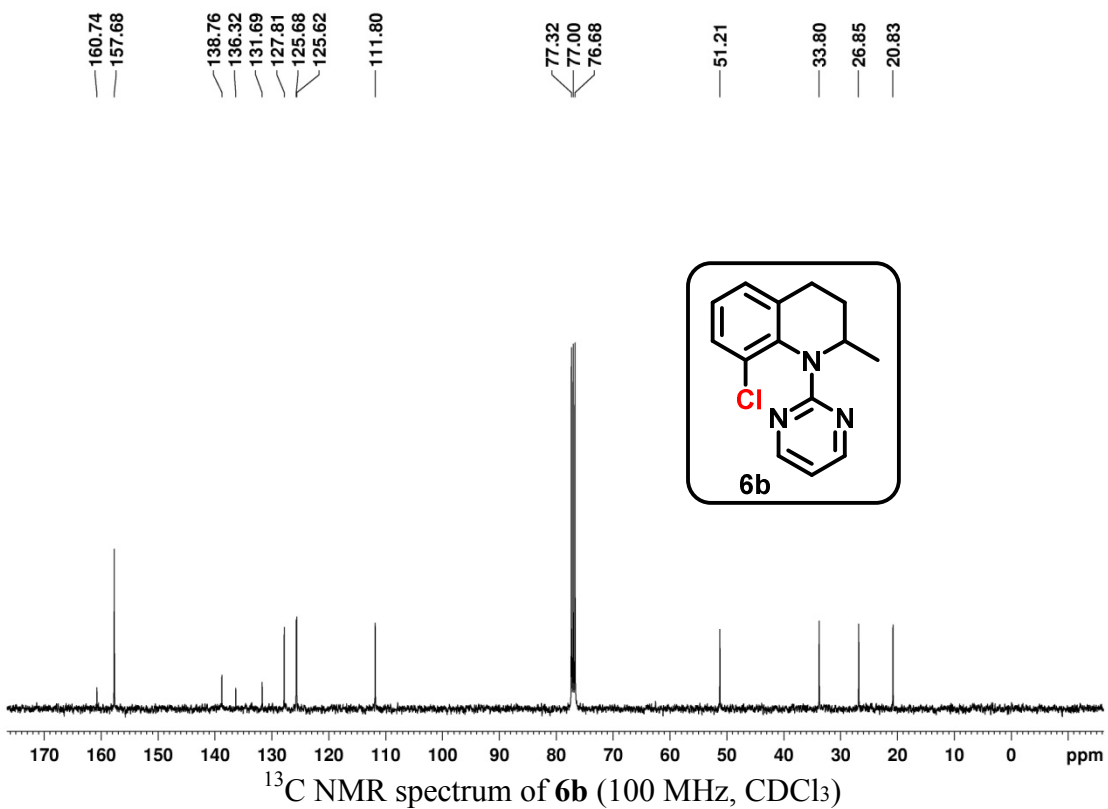
^{13}C NMR spectrum of **2m** (100 MHz, CDCl_3)



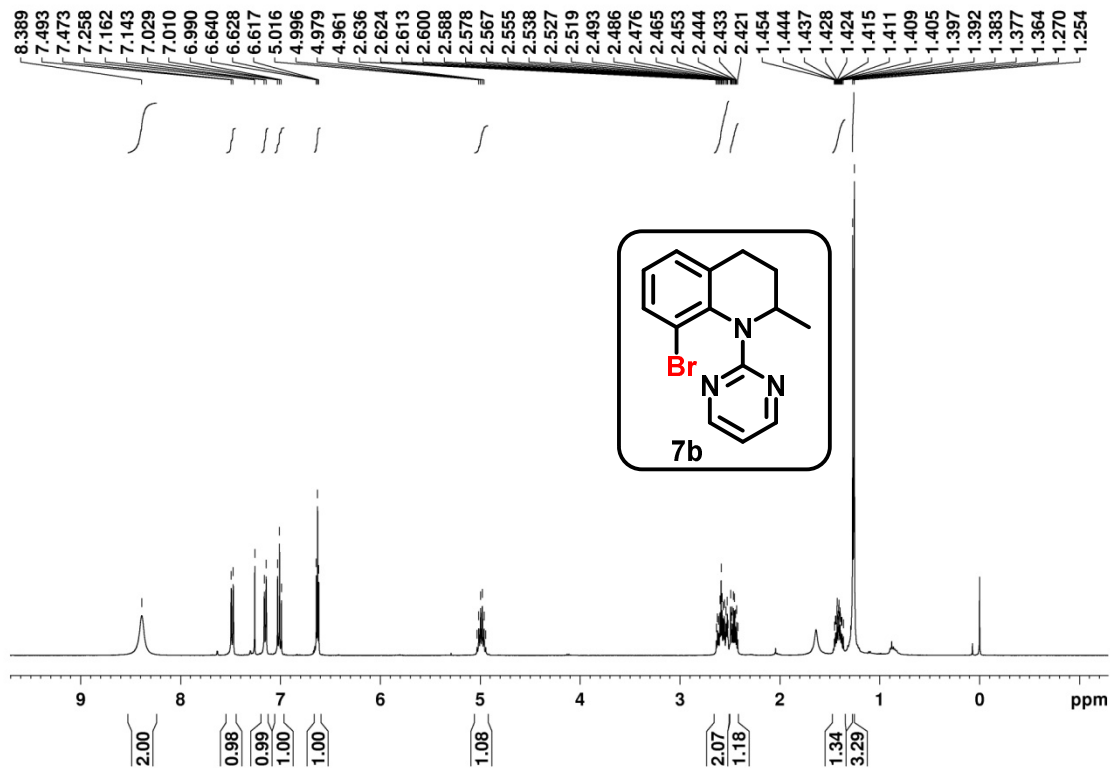




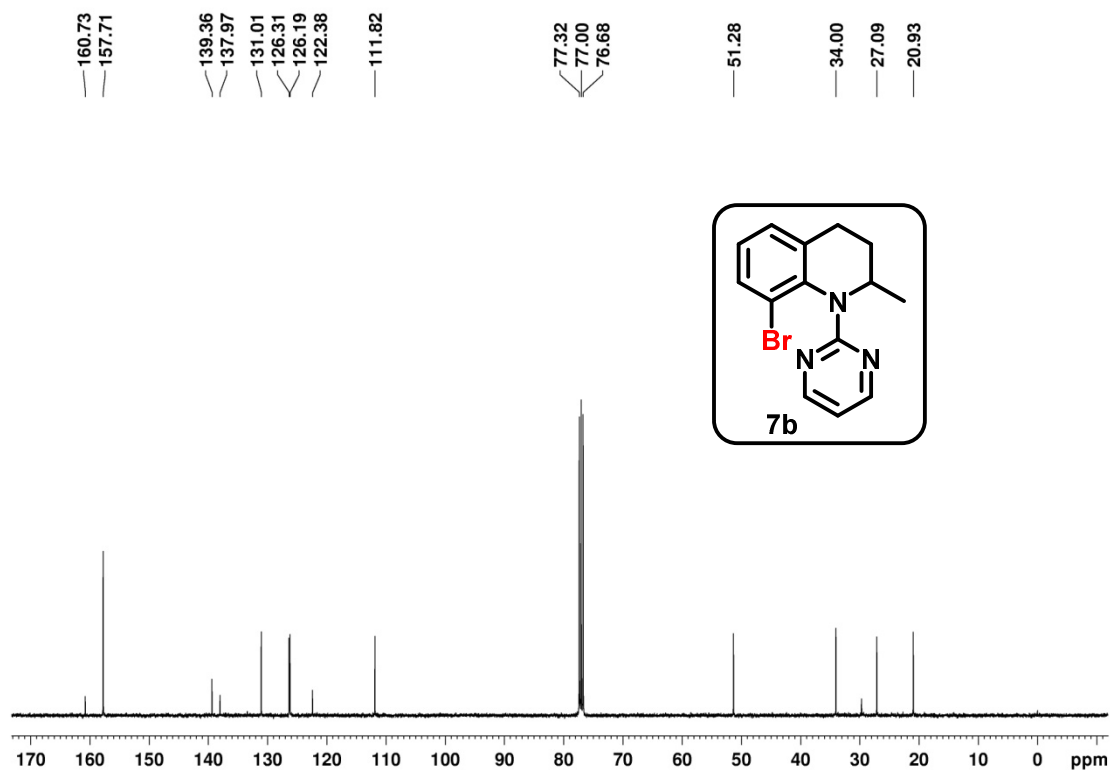
^1H NMR spectrum of **6b** (400 MHz, CDCl_3)



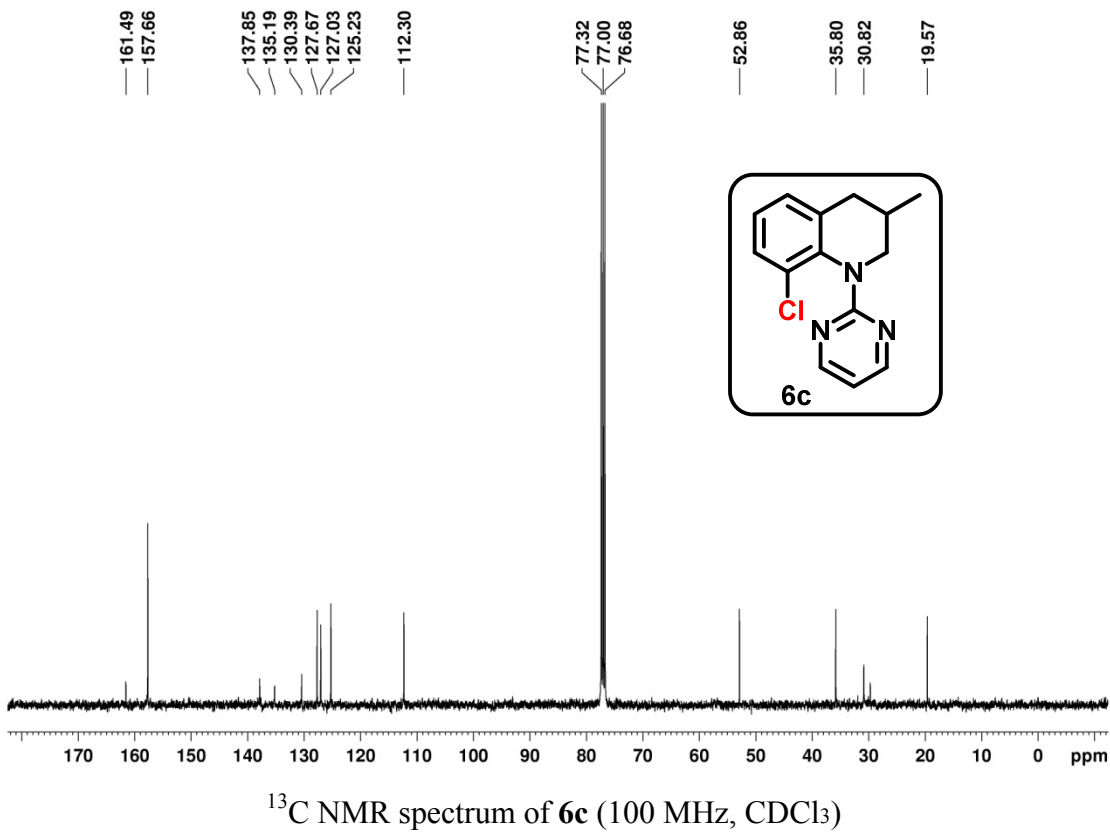
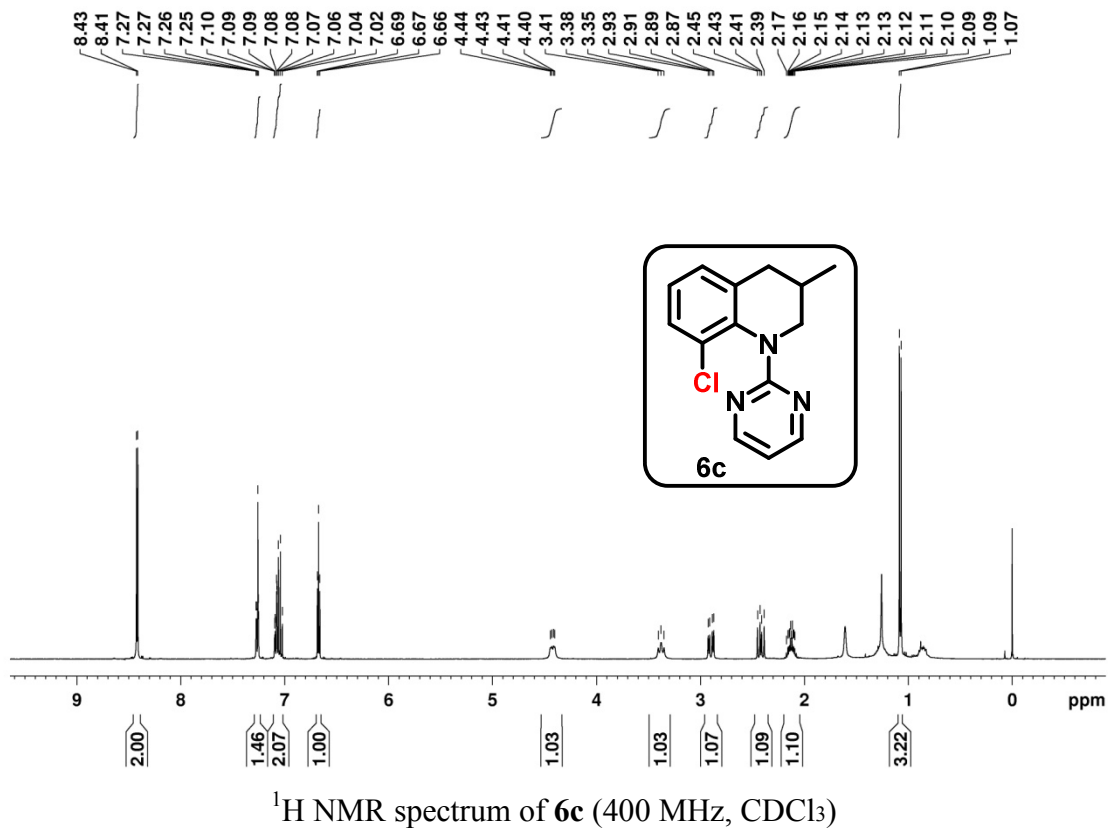
^{13}C NMR spectrum of **6b** (100 MHz, CDCl_3)

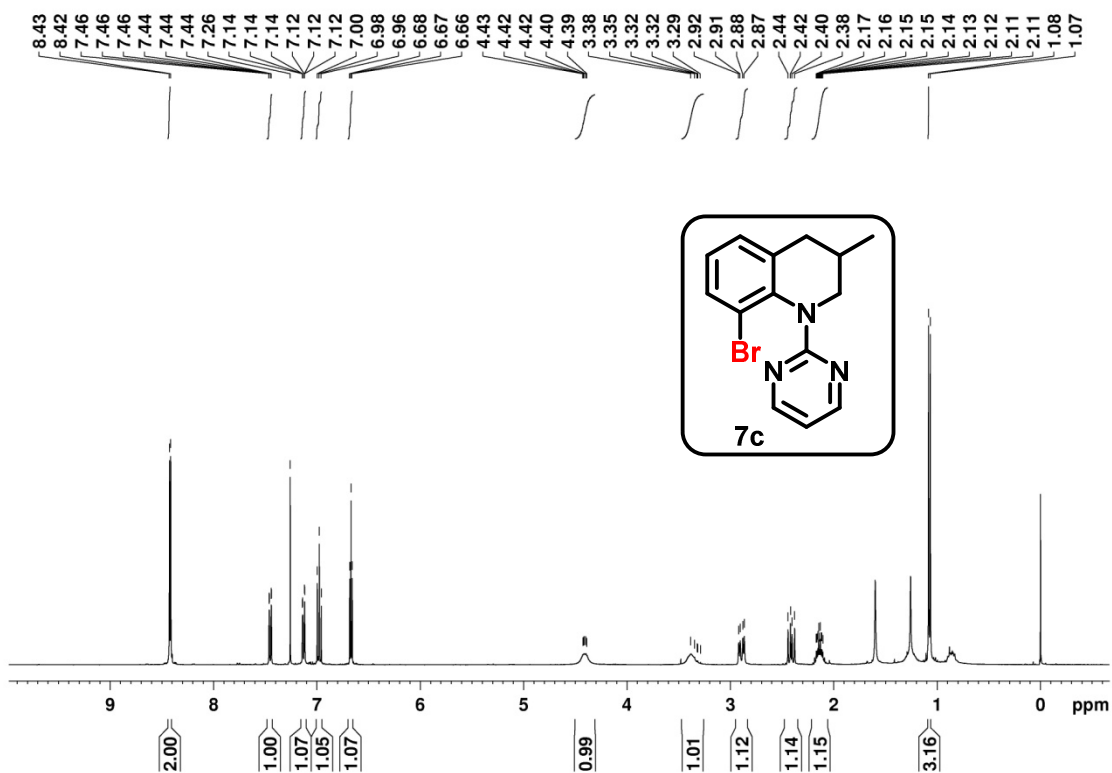


¹H NMR spectrum of **7b** (400 MHz, CDCl₃)

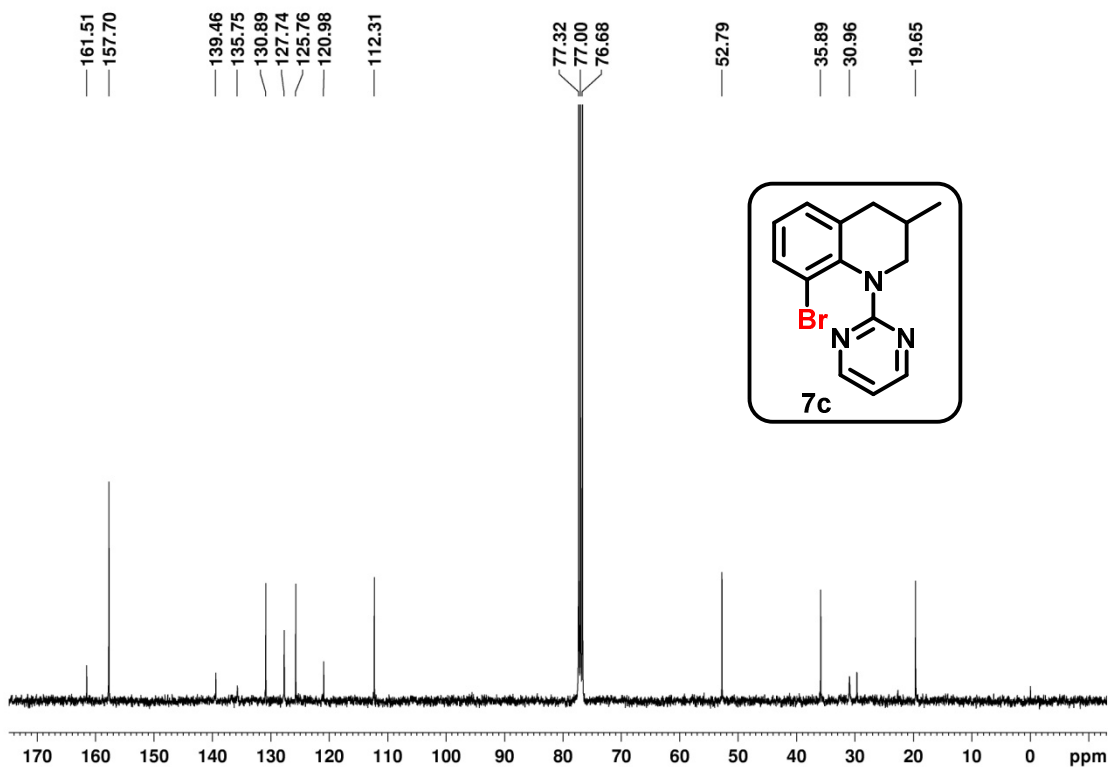


¹³C NMR spectrum of **7b** (100 MHz, CDCl₃)

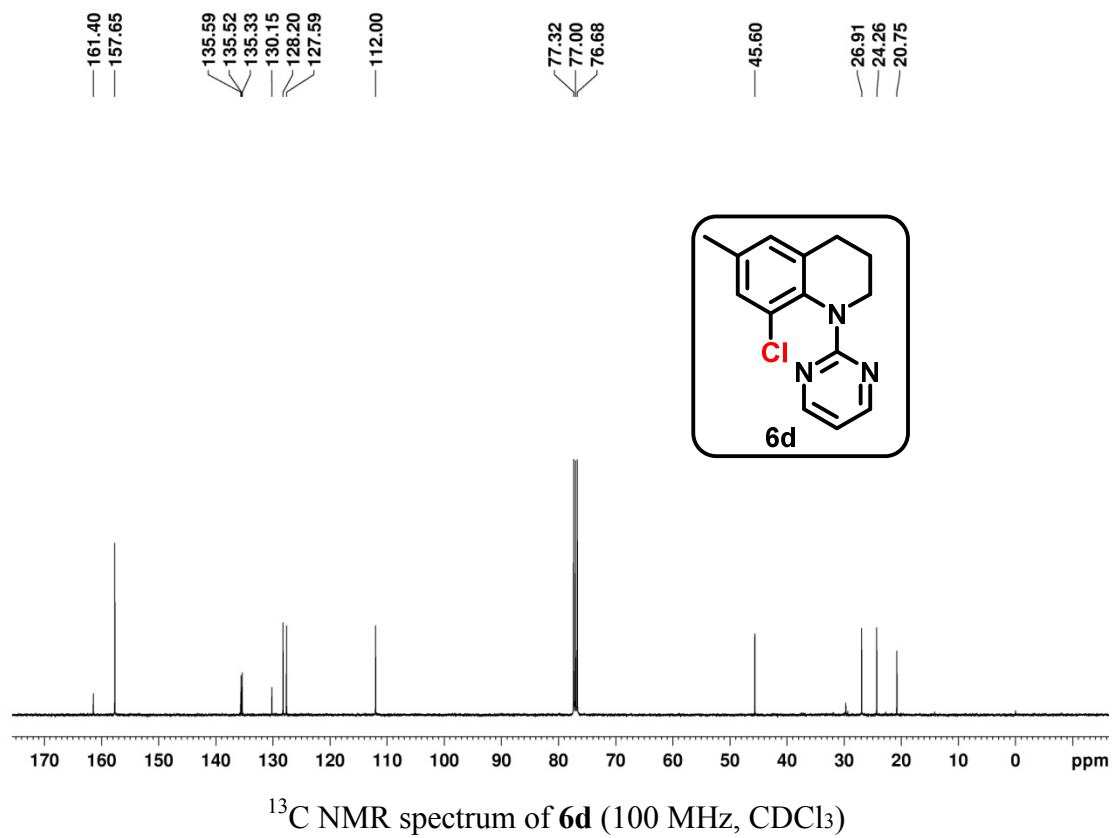
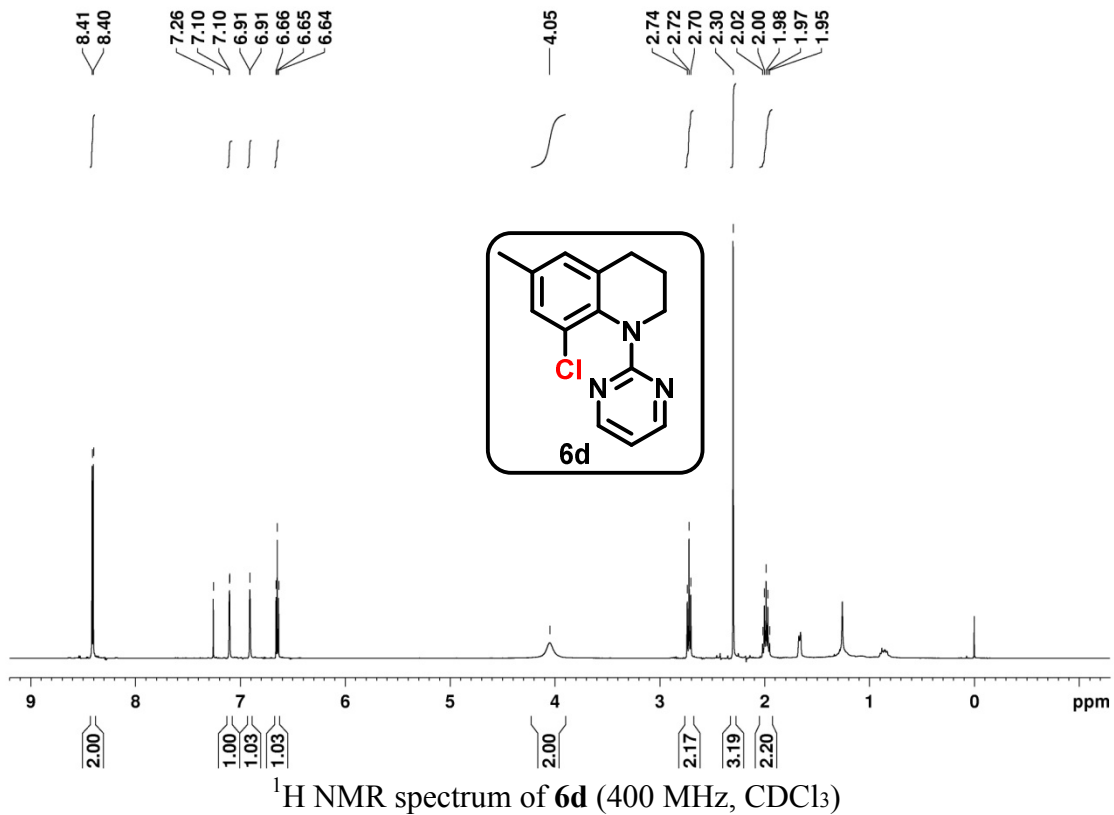


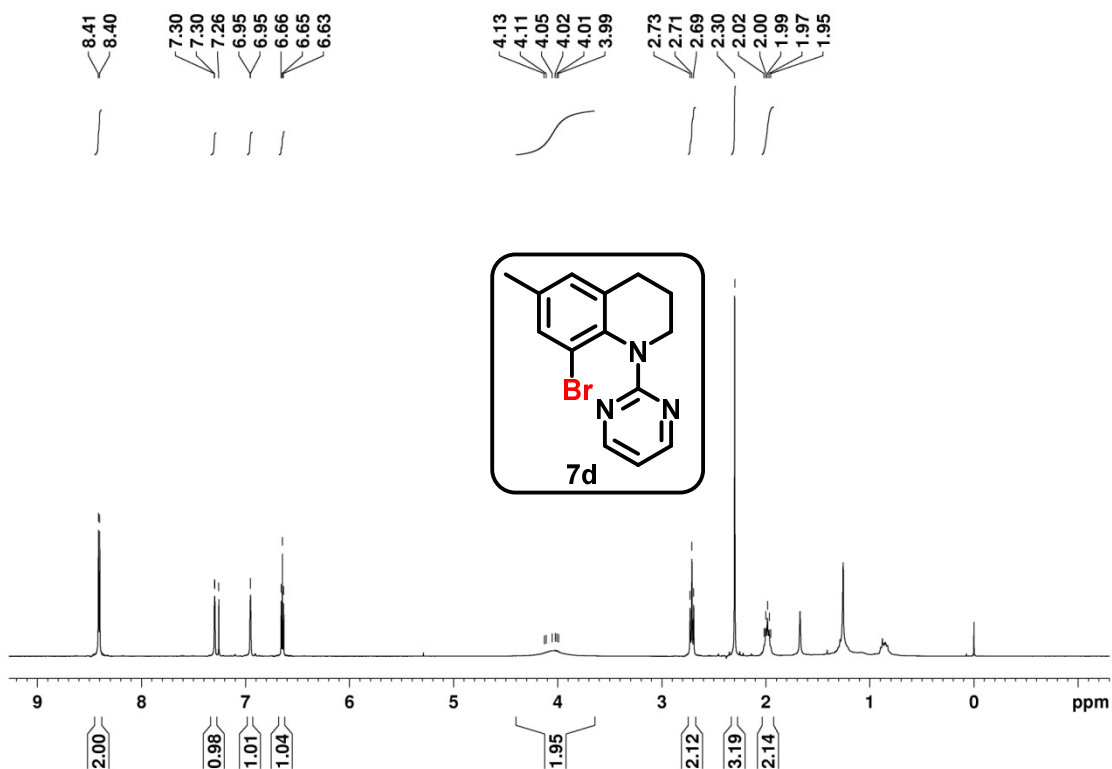


^1H NMR spectrum of **7c** (400 MHz, CDCl_3)

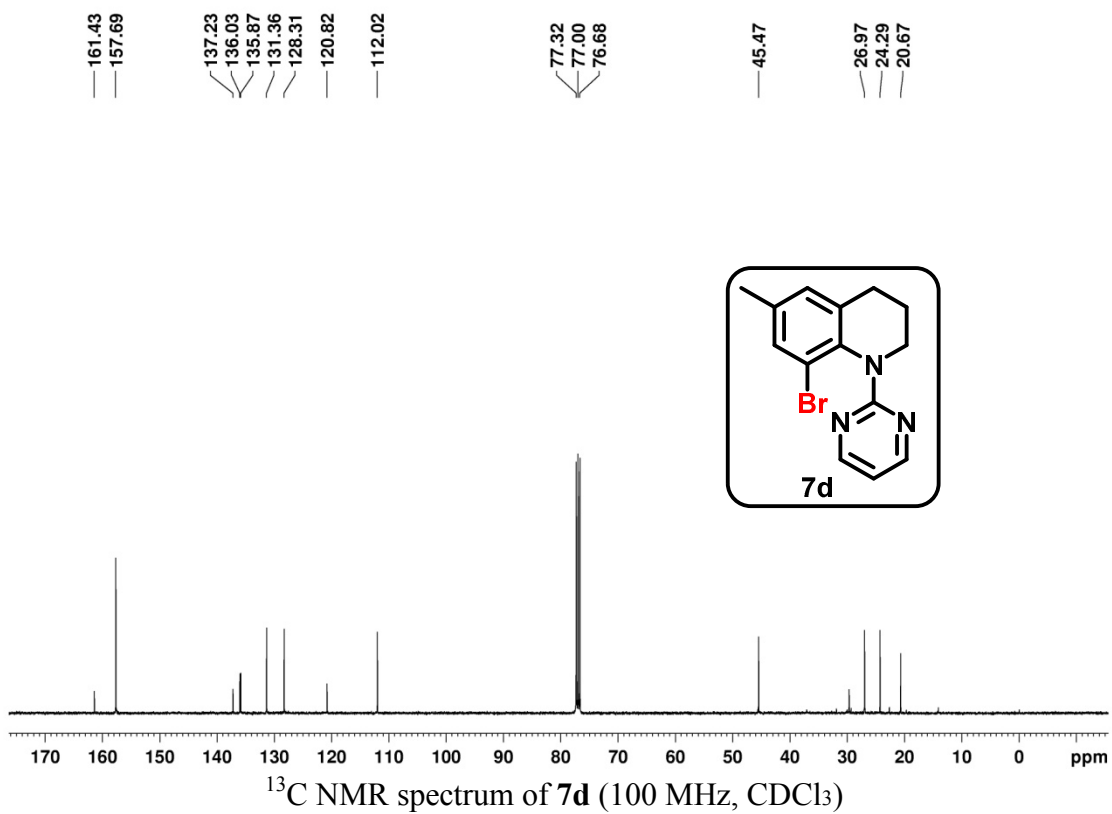


^{13}C NMR spectrum of **7c** (100 MHz, CDCl_3)

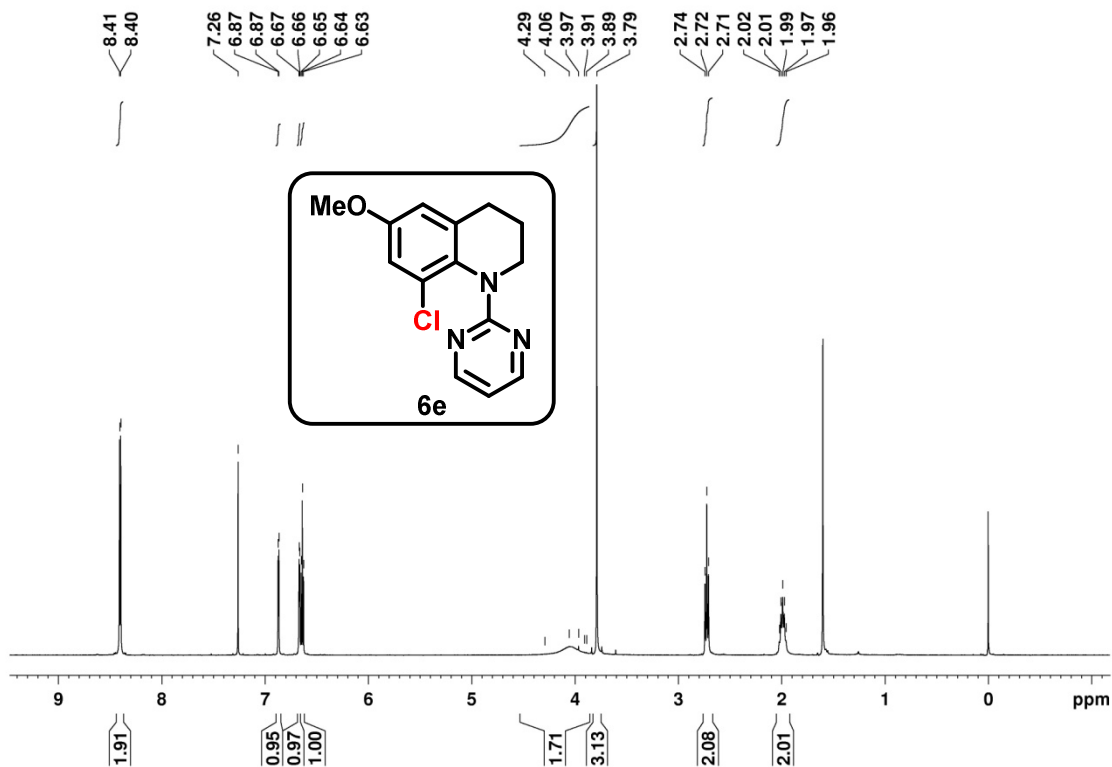




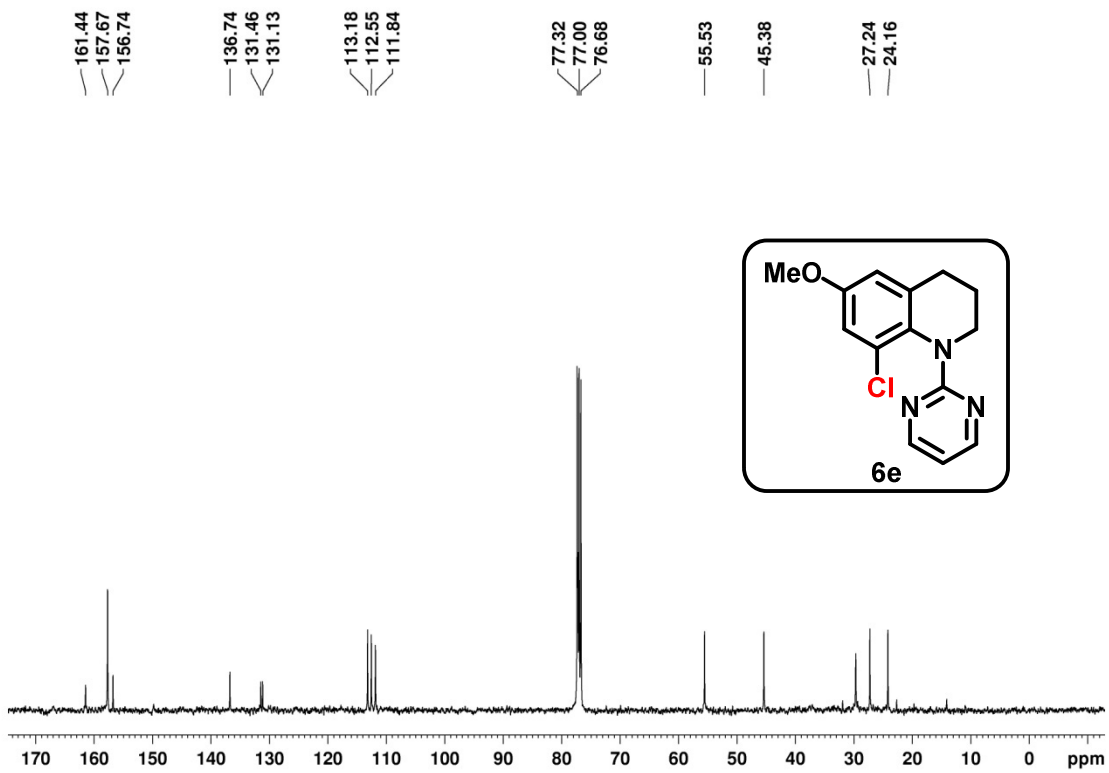
¹H NMR spectrum of **7d** (400 MHz, CDCl₃)



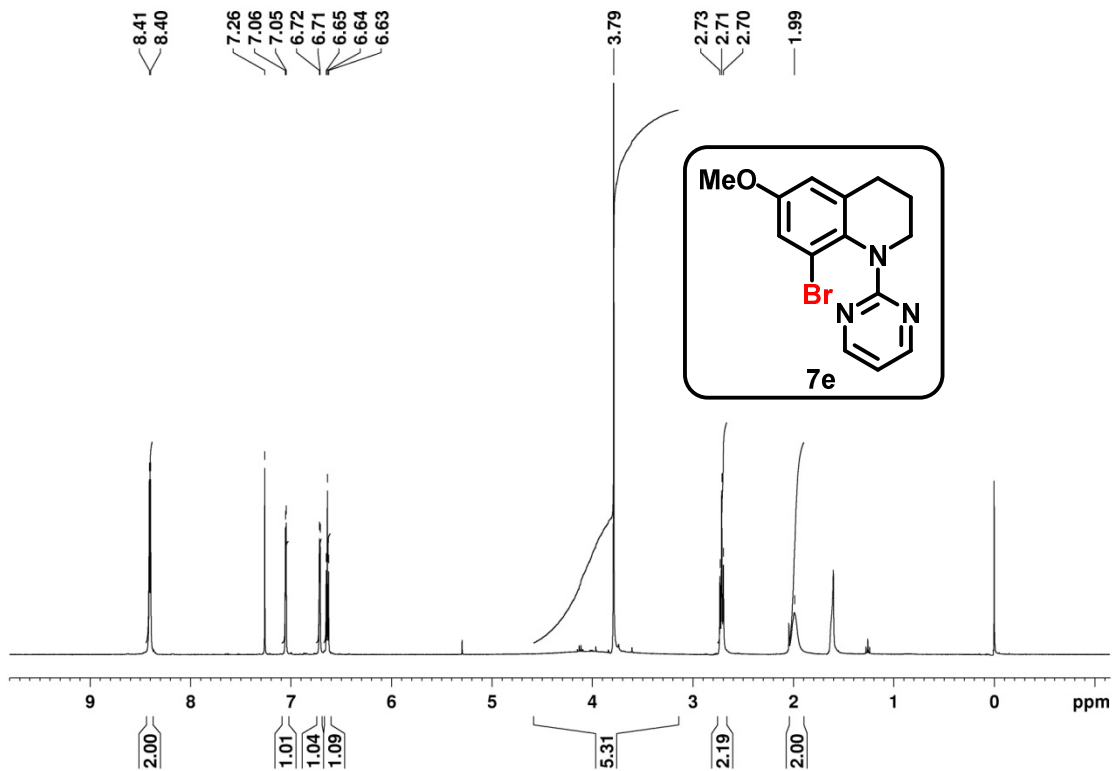
¹³C NMR spectrum of **7d** (100 MHz, CDCl₃)



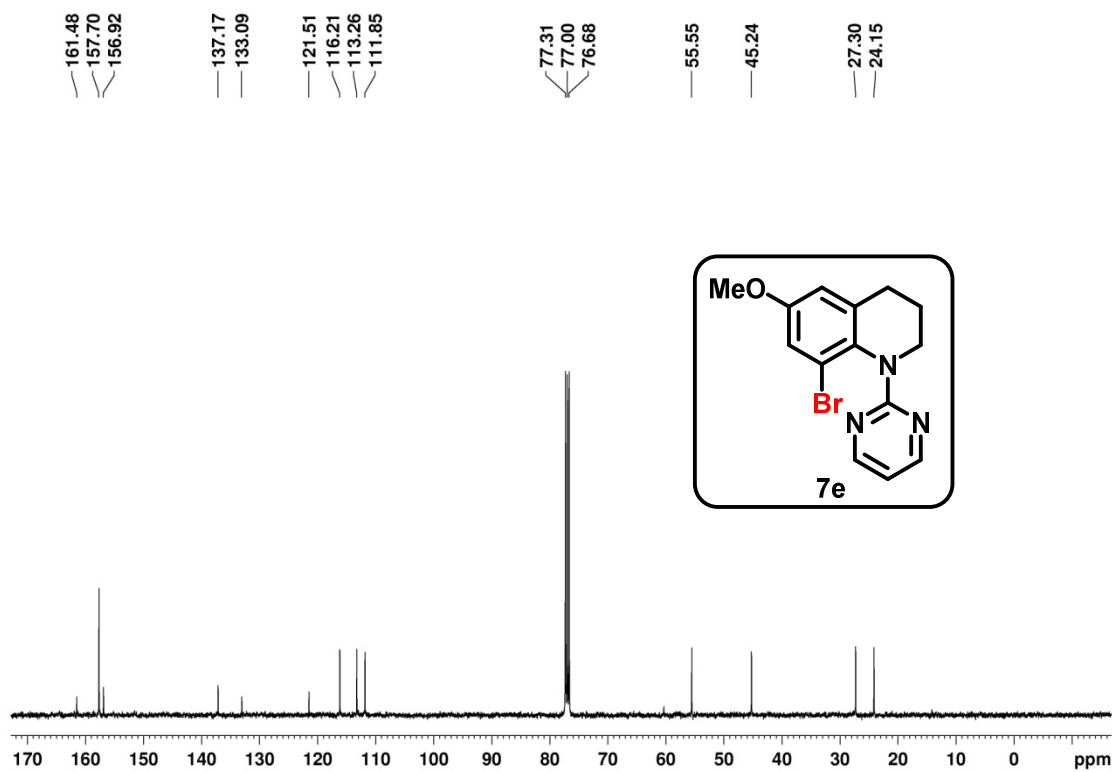
^1H NMR spectrum of **6e** (400 MHz, CDCl_3)



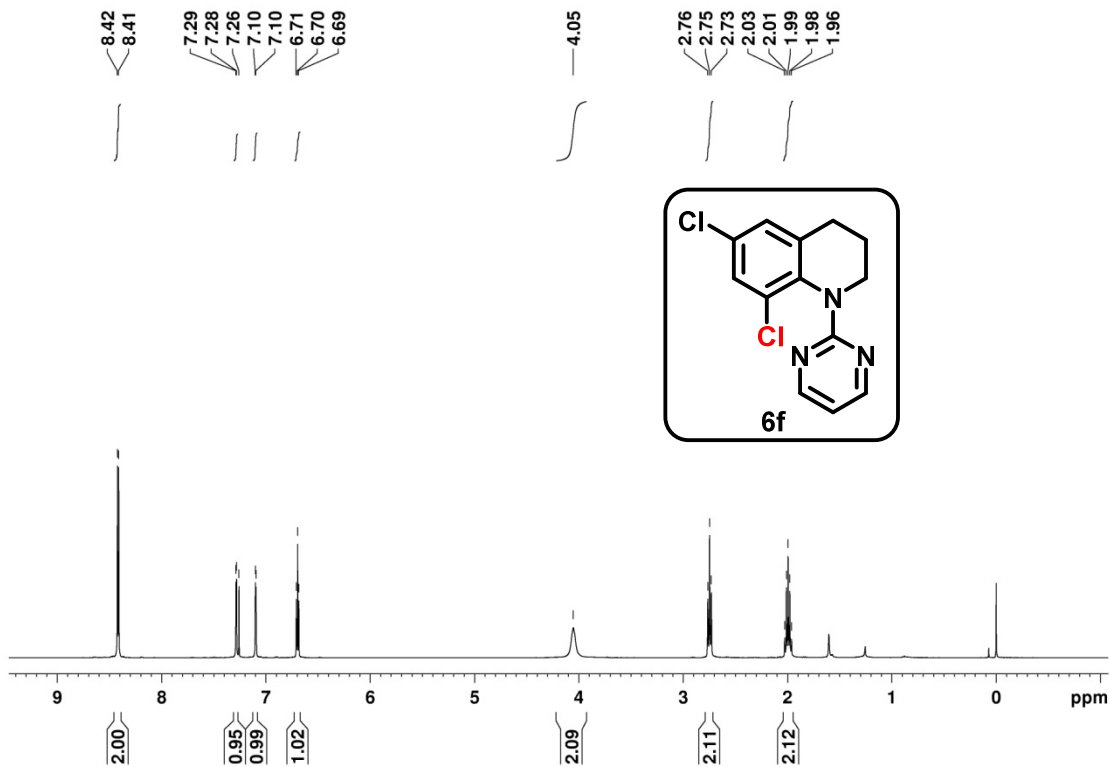
^{13}C NMR spectrum of **6e** (100 MHz, CDCl_3)



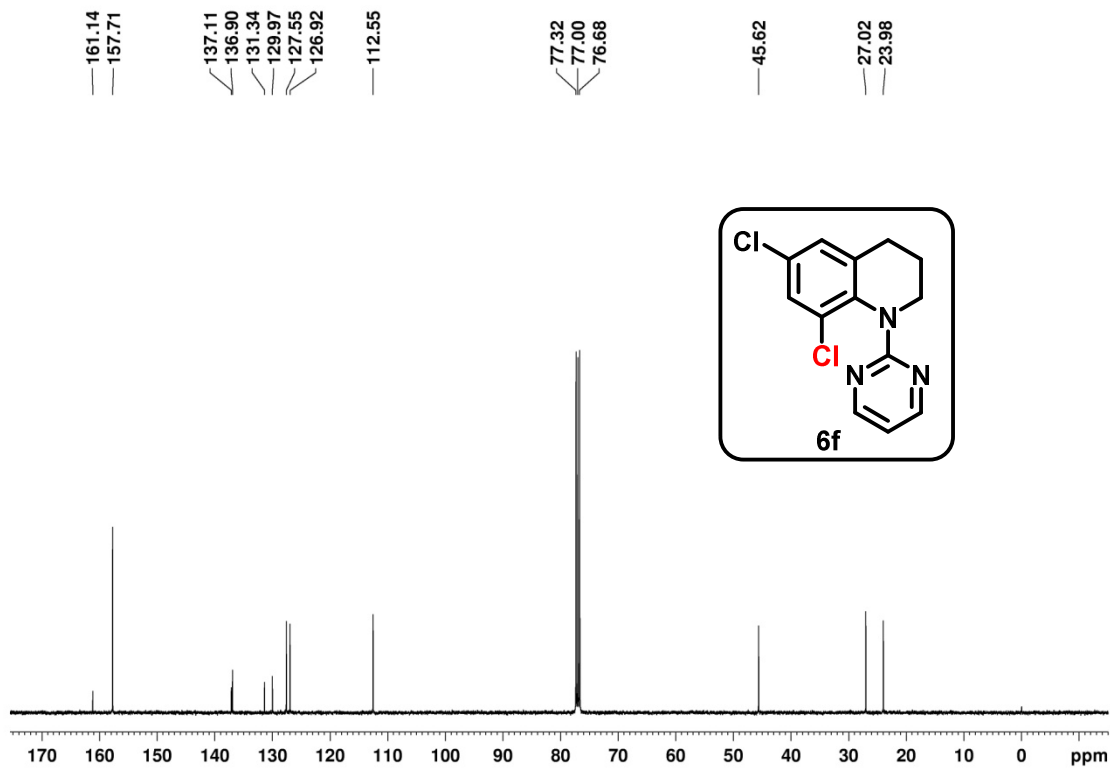
^1H NMR spectrum of **7e** (400 MHz, CDCl_3)



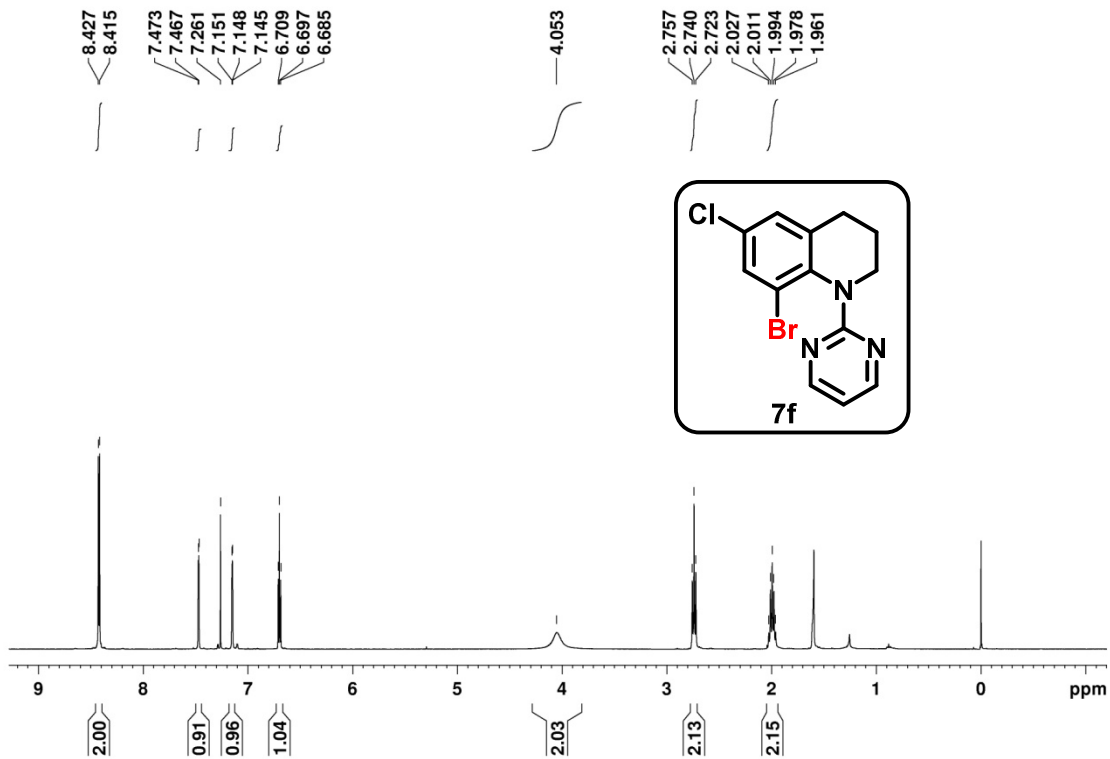
^{13}C NMR spectrum of **7e** (100 MHz, CDCl_3)



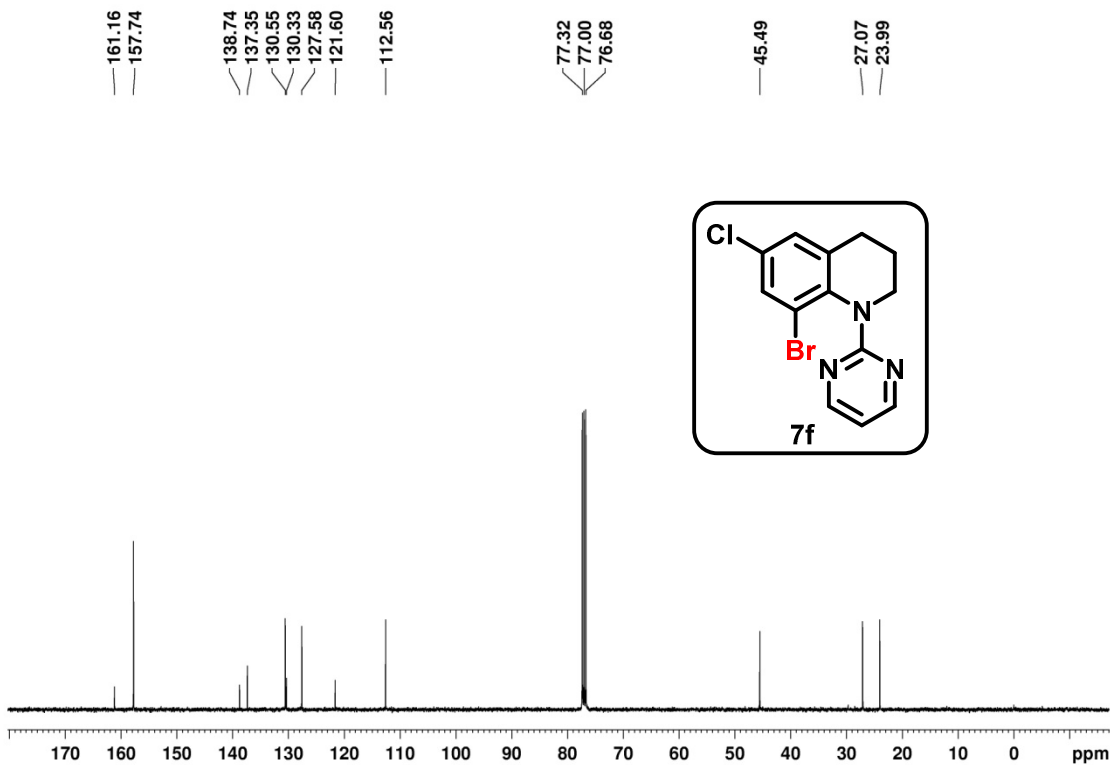
¹H NMR spectrum of **6f** (400 MHz, CDCl₃)



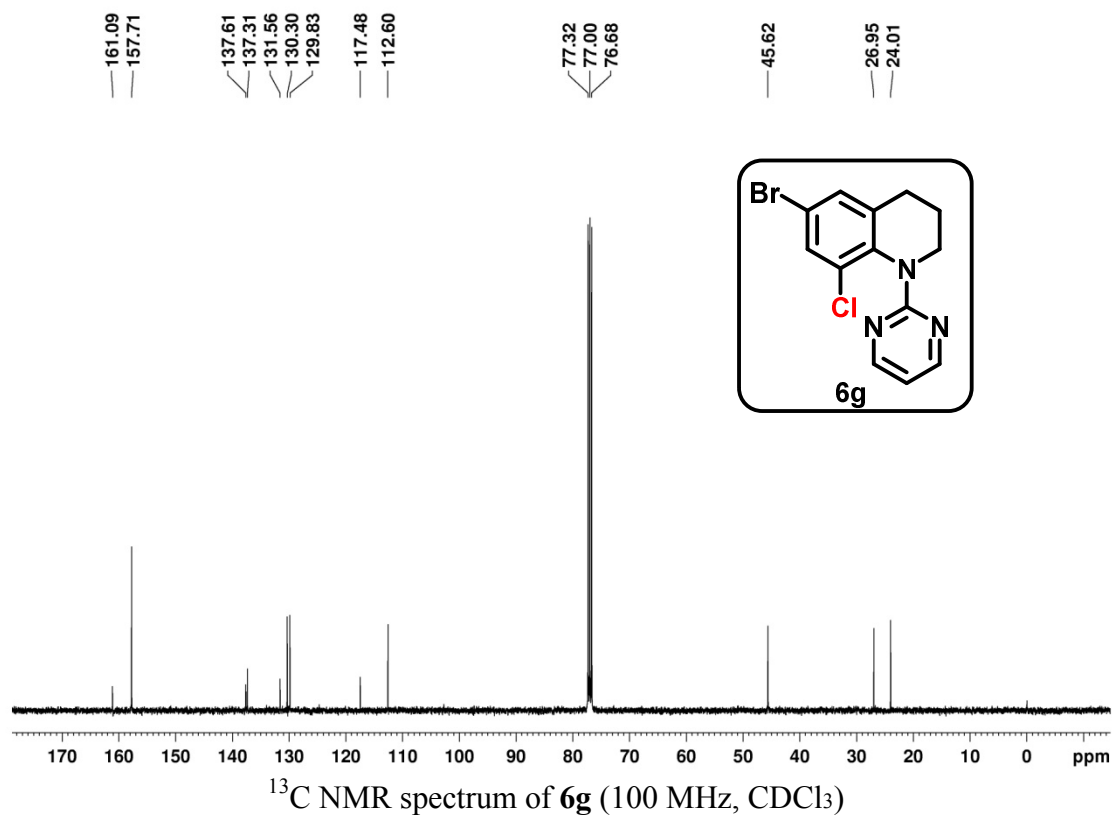
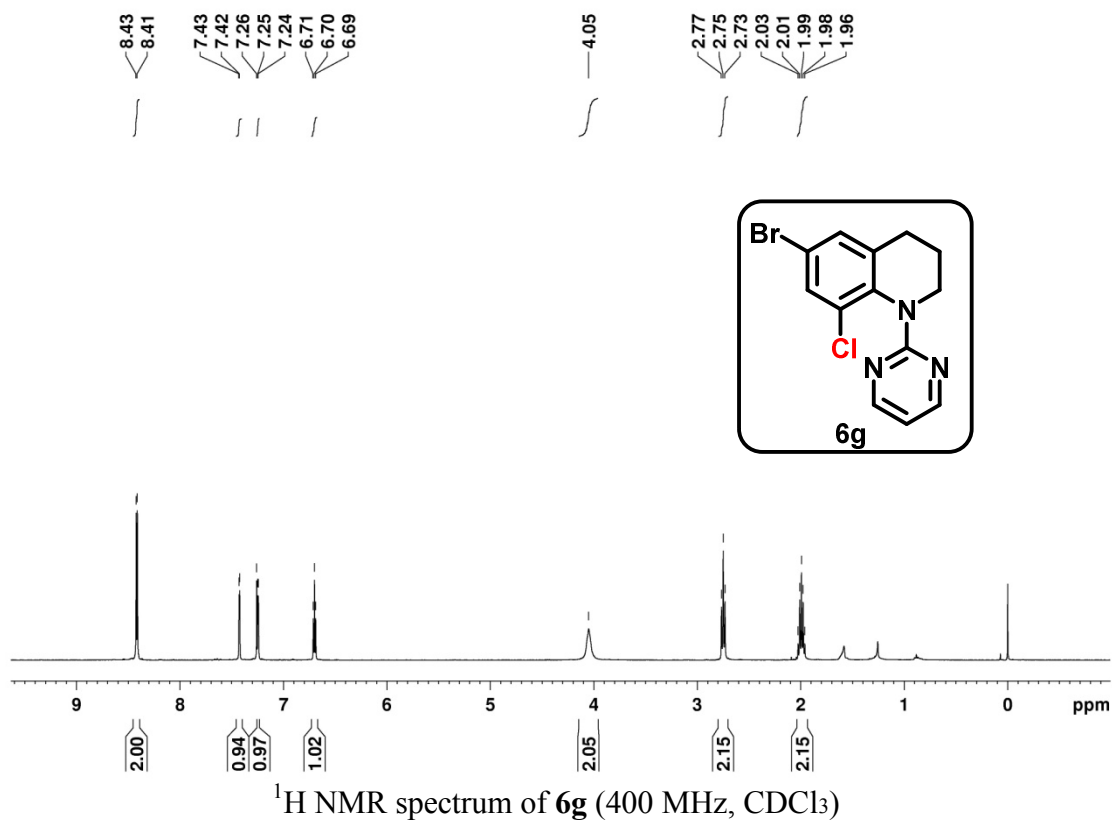
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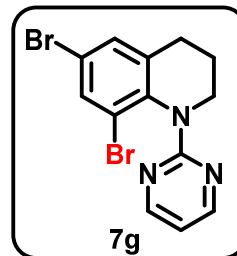
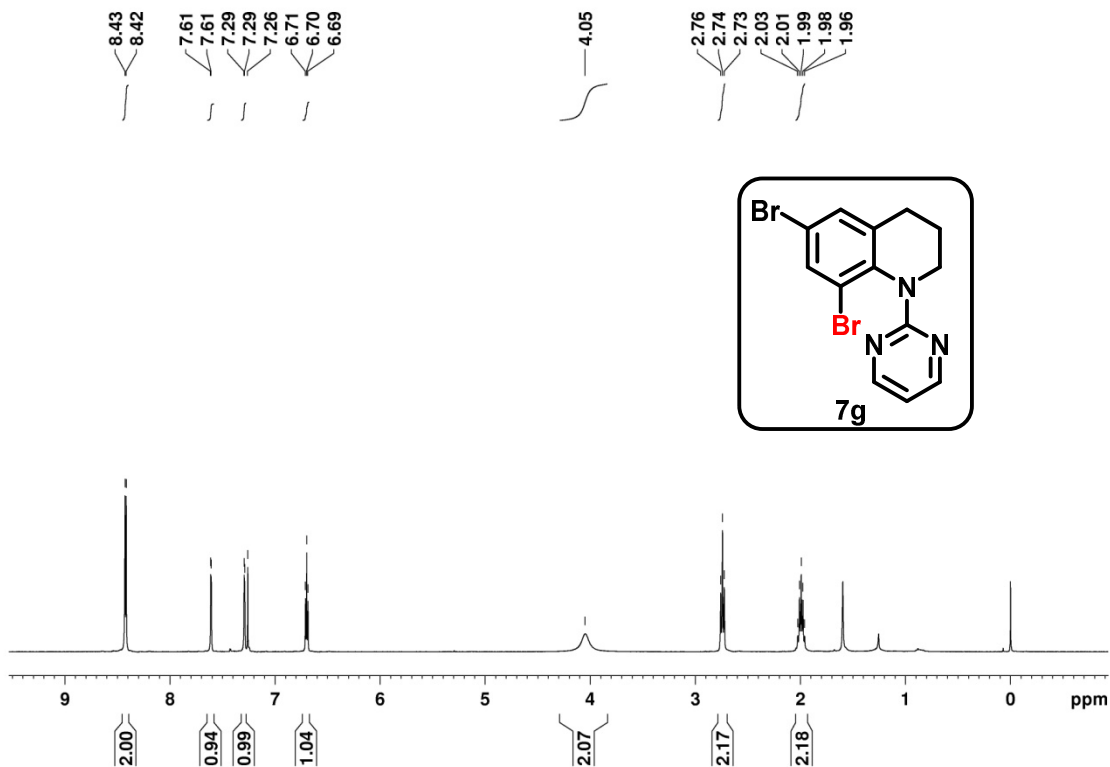


^1H NMR spectrum of **7f** (400 MHz, CDCl_3)

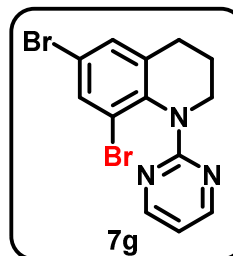
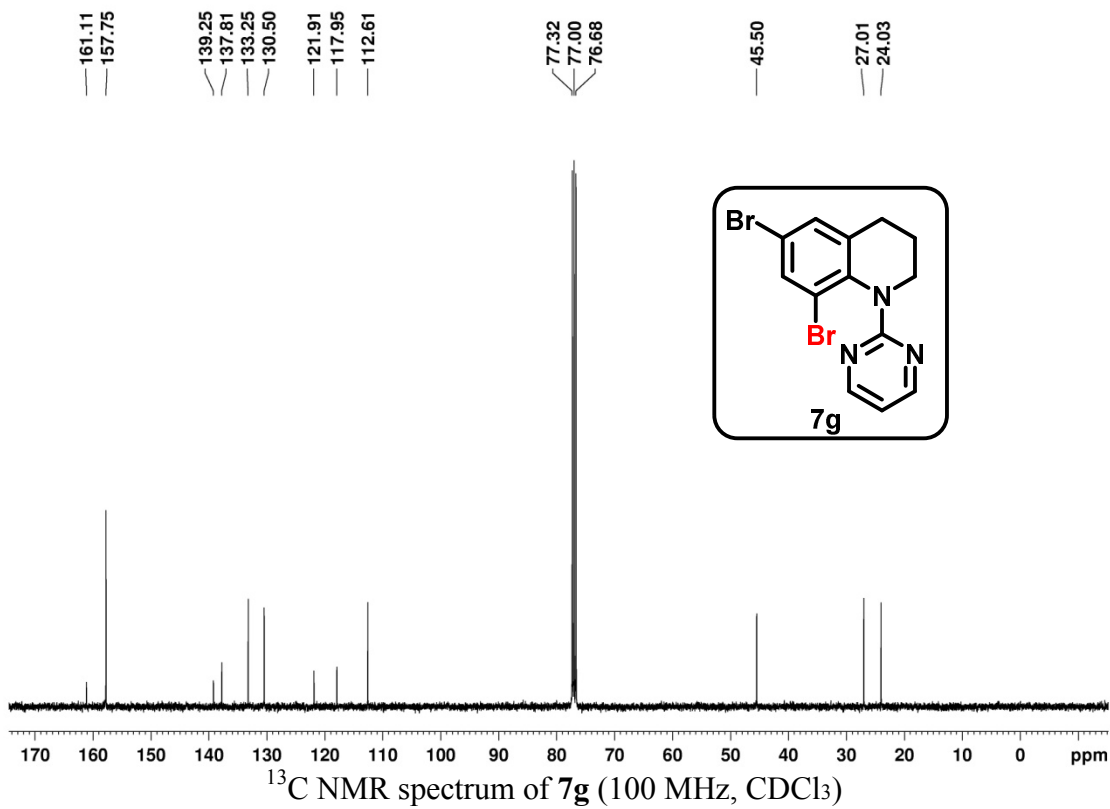


^{13}C NMR spectrum of **7f** (100 MHz, CDCl_3)

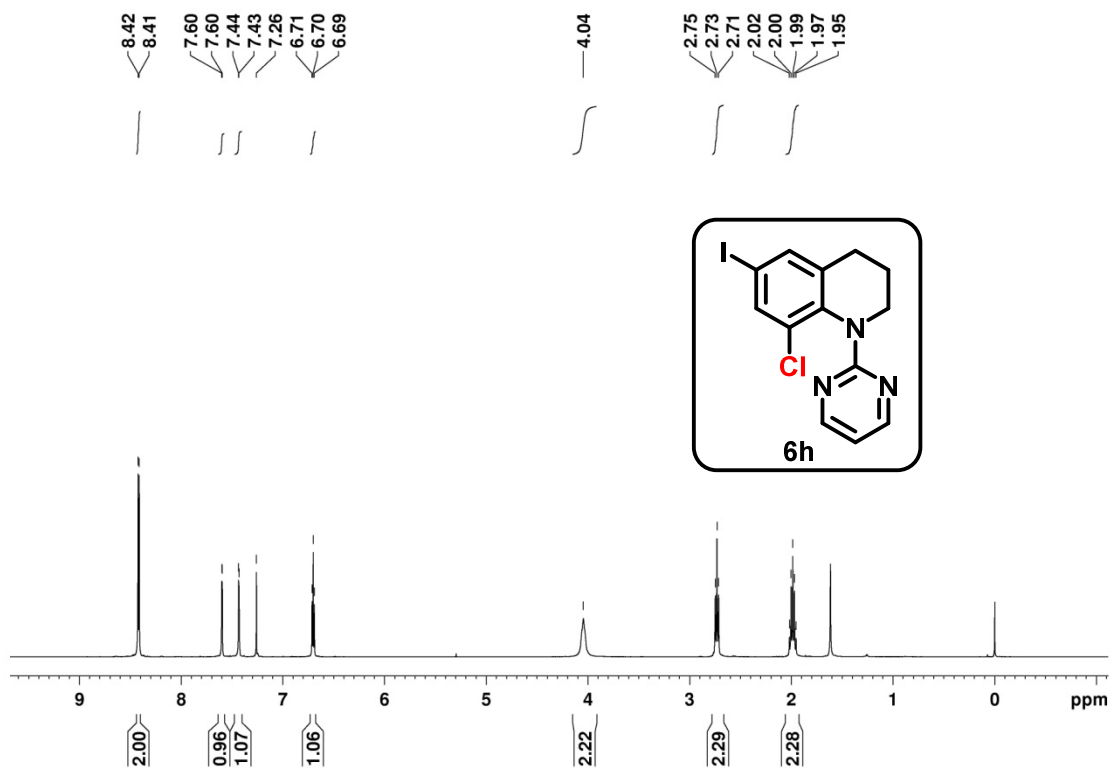




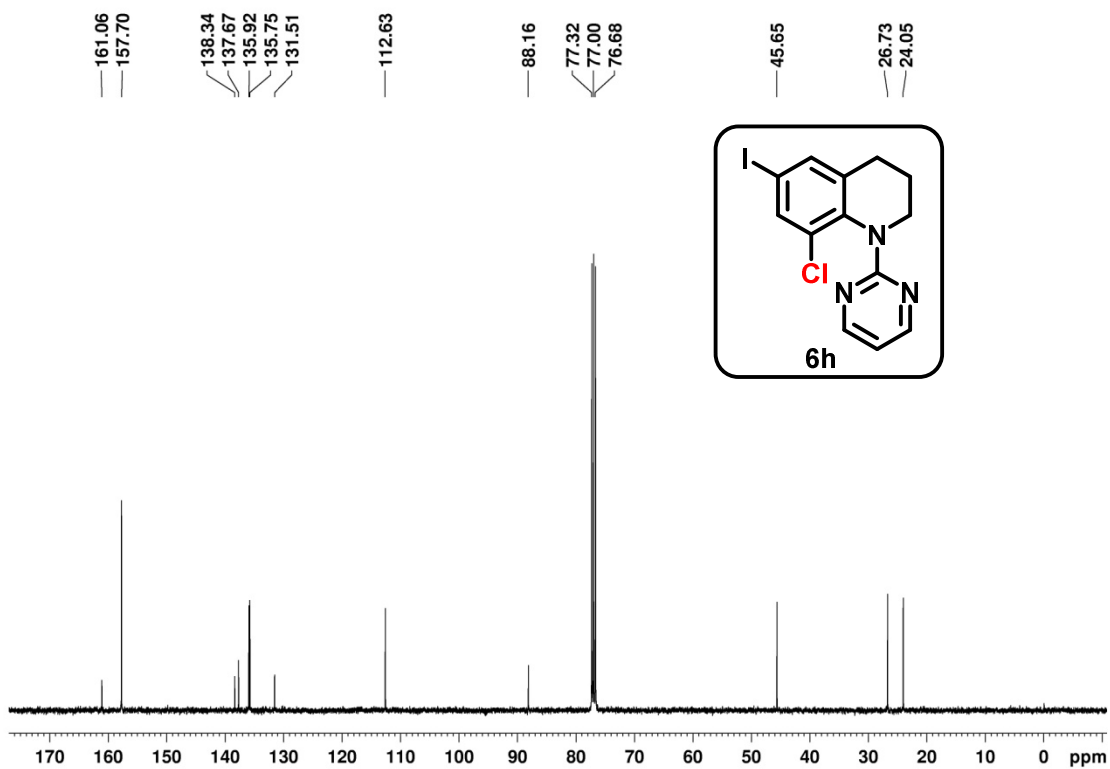
^1H NMR spectrum of **7g** (400 MHz, CDCl_3)



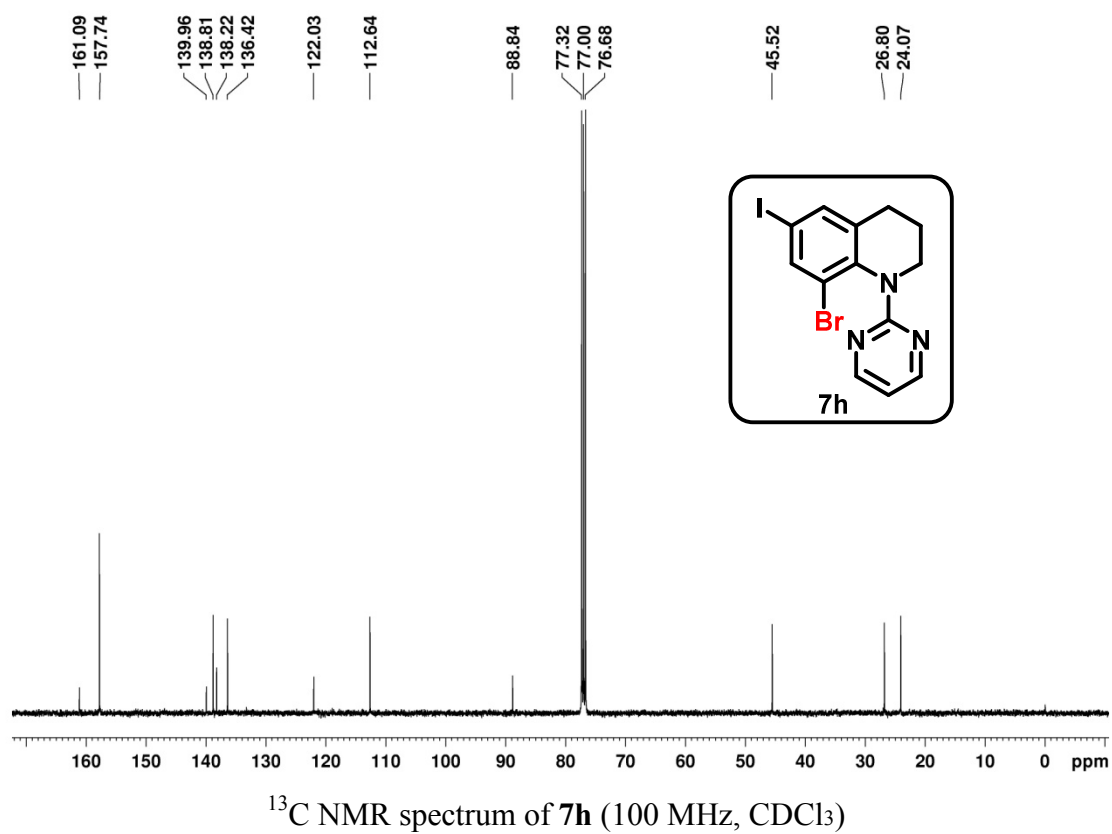
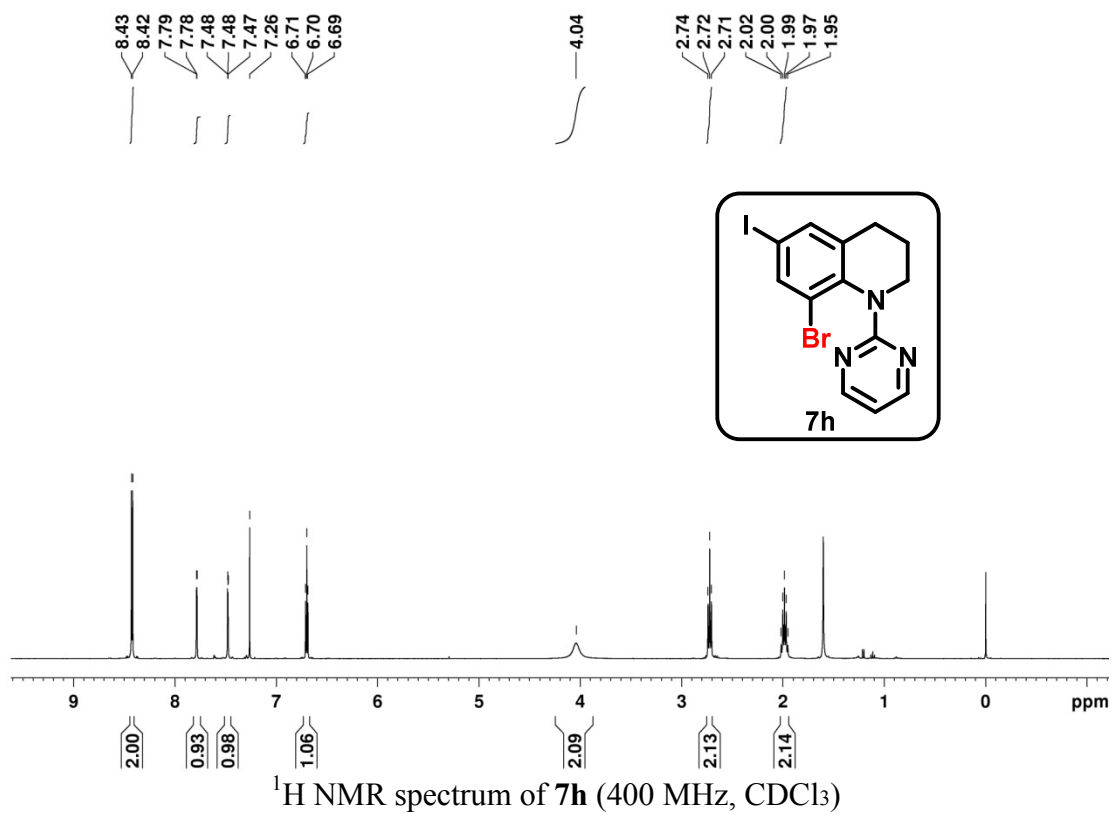
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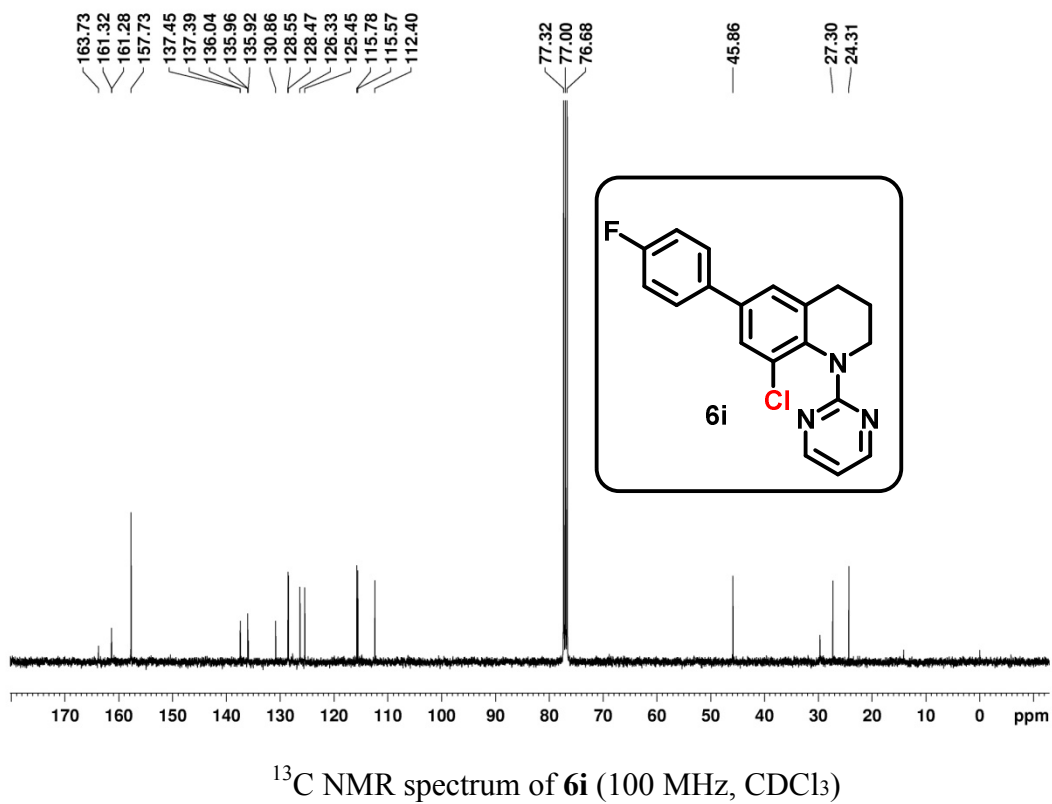
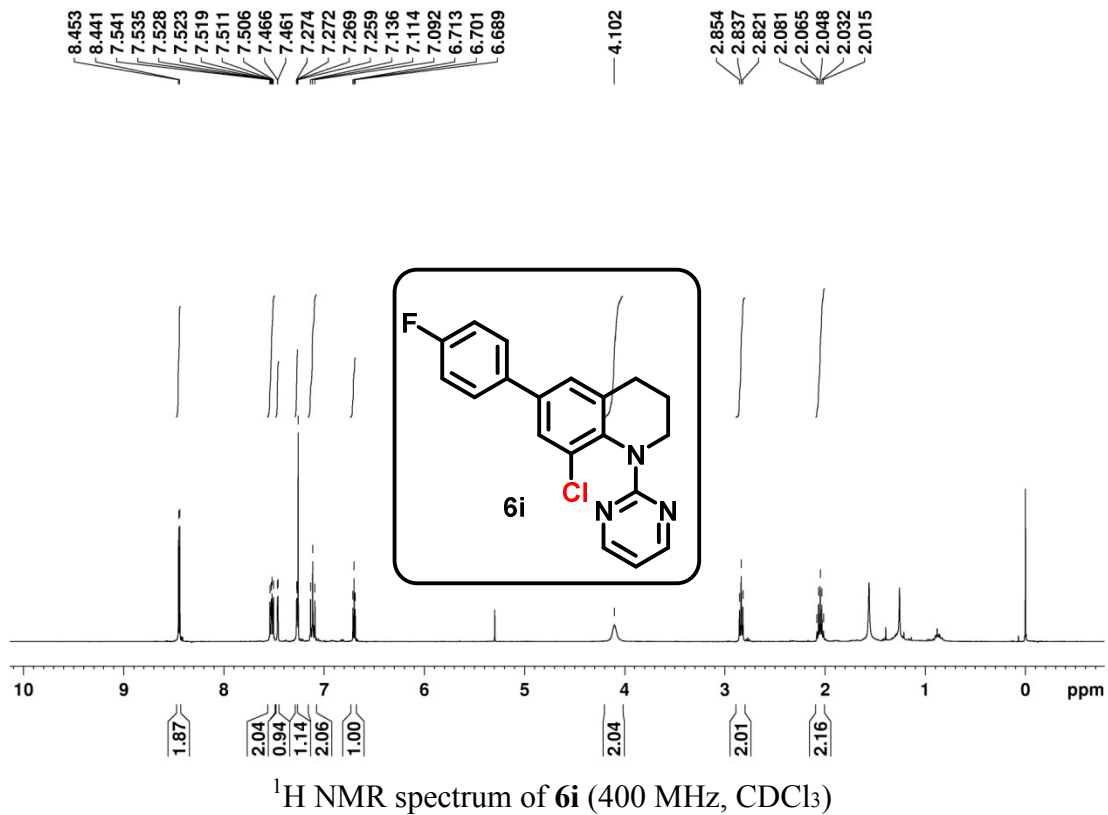


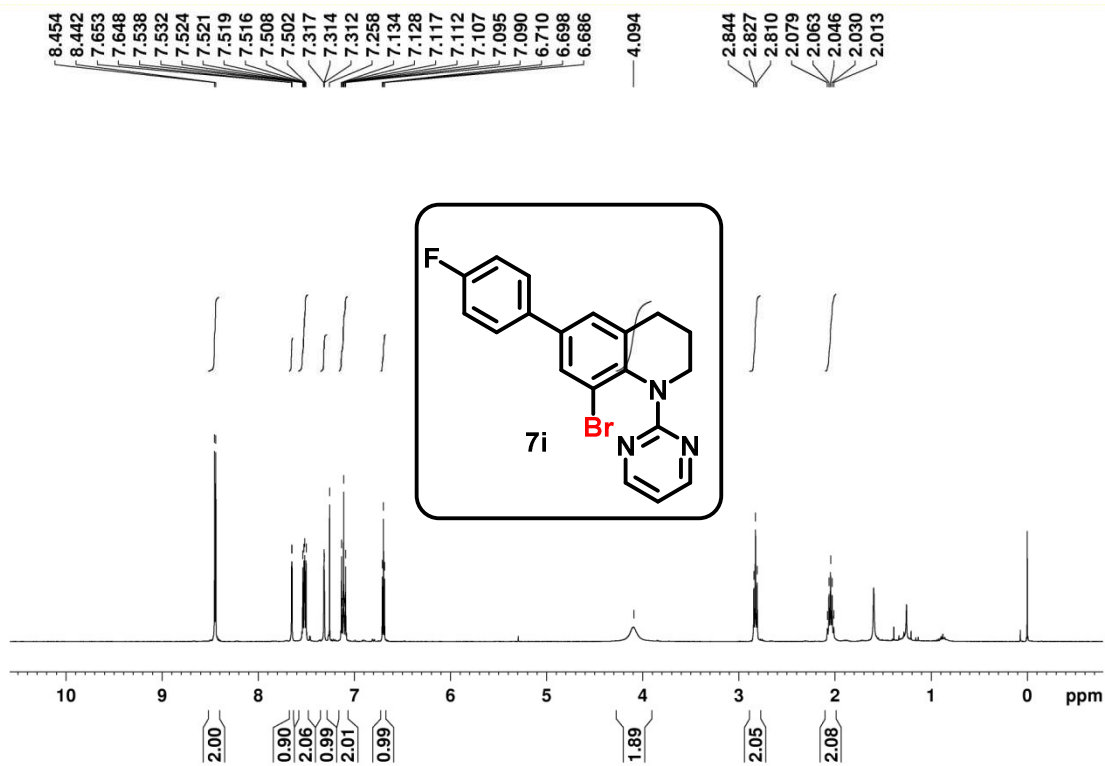
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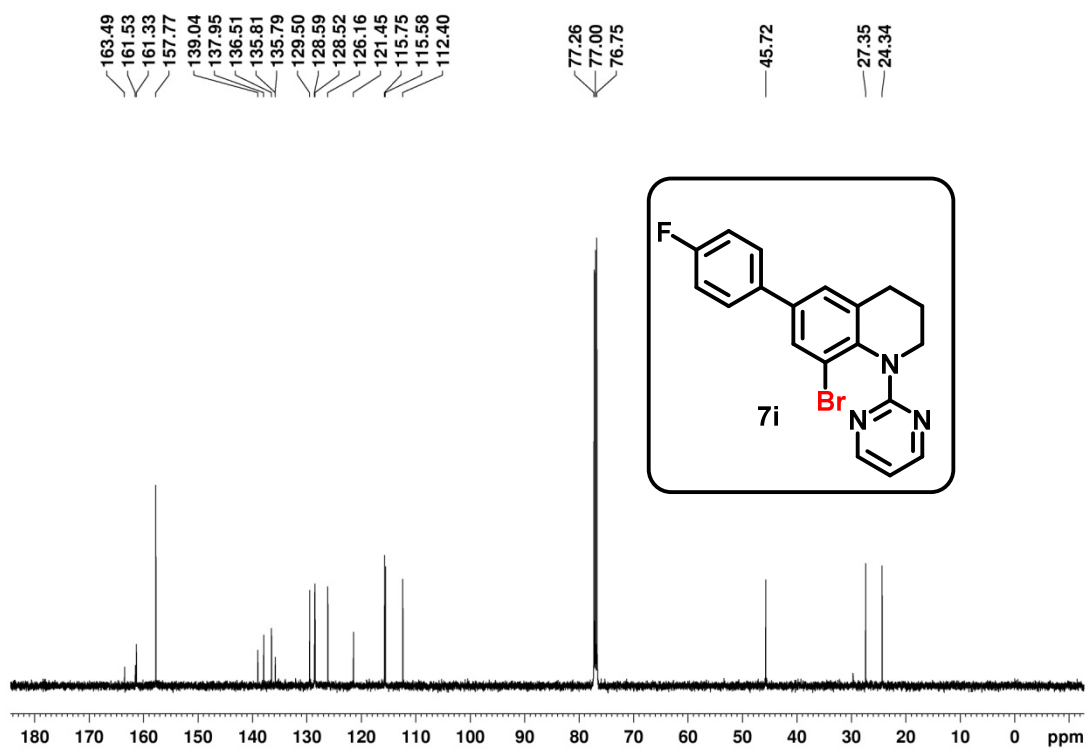
¹³C NMR spectrum of **6h** (100 MHz, CDCl₃)



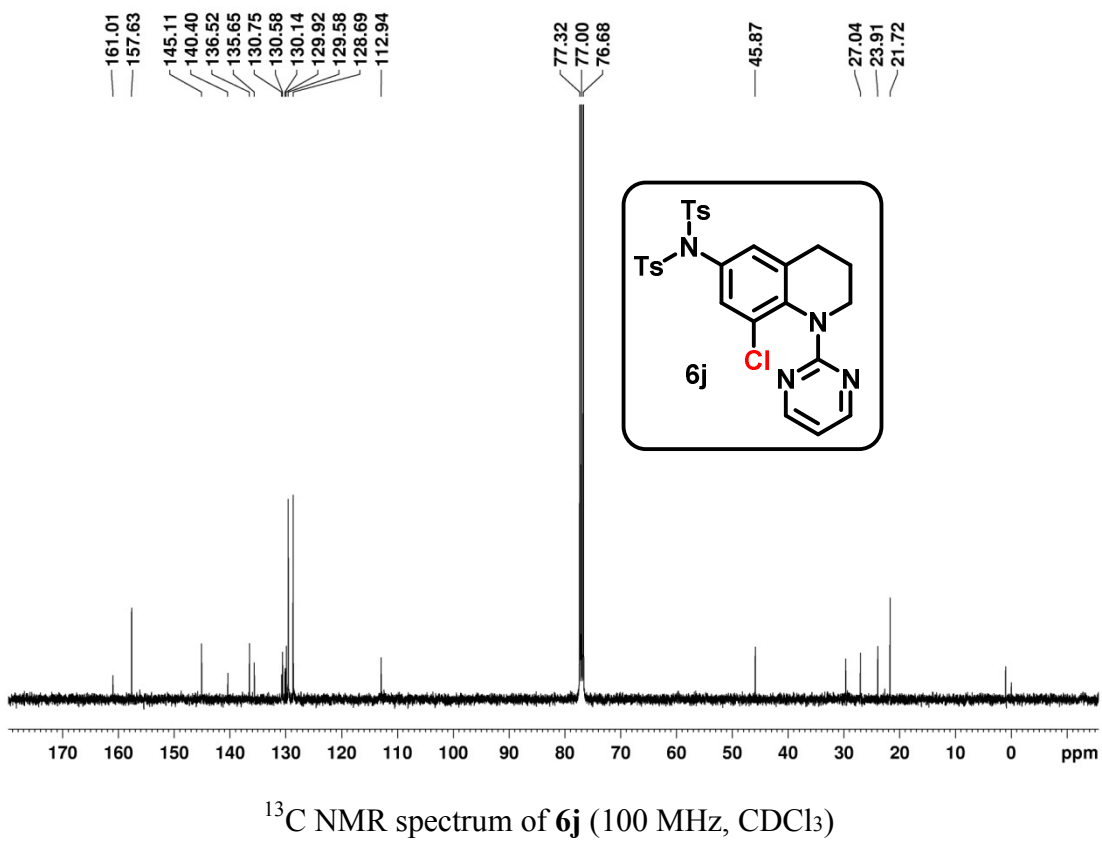
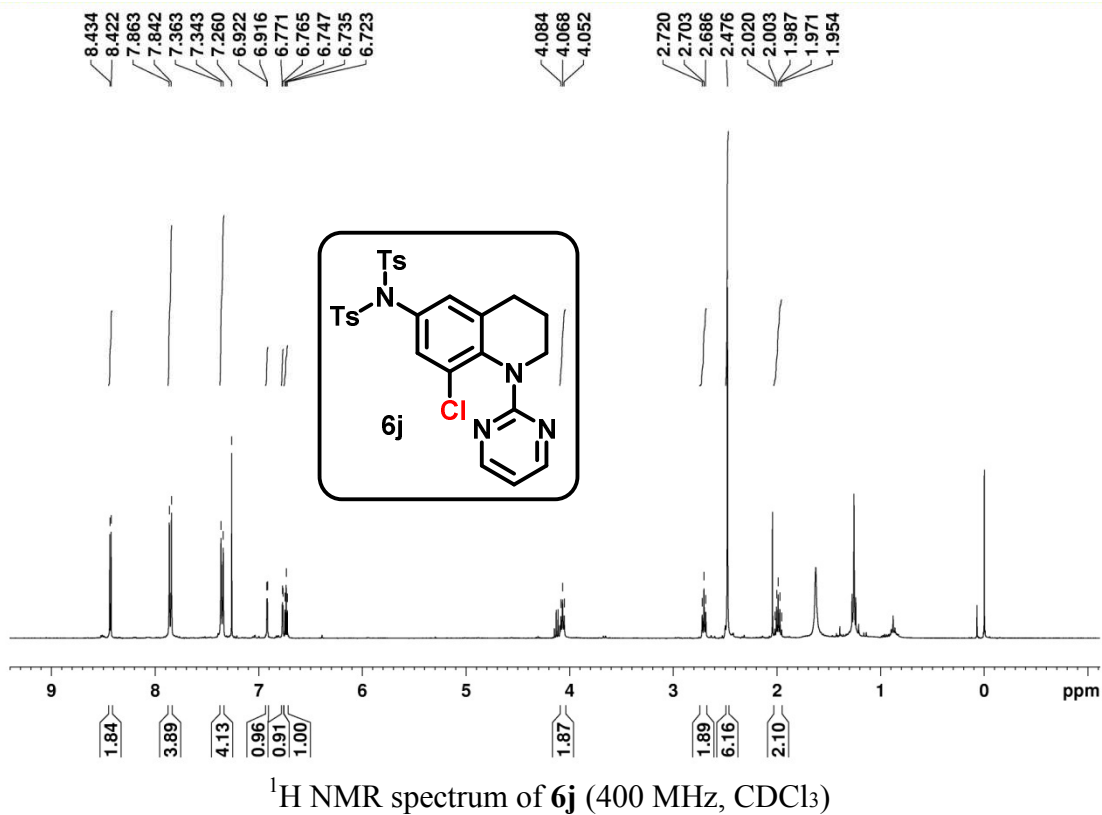


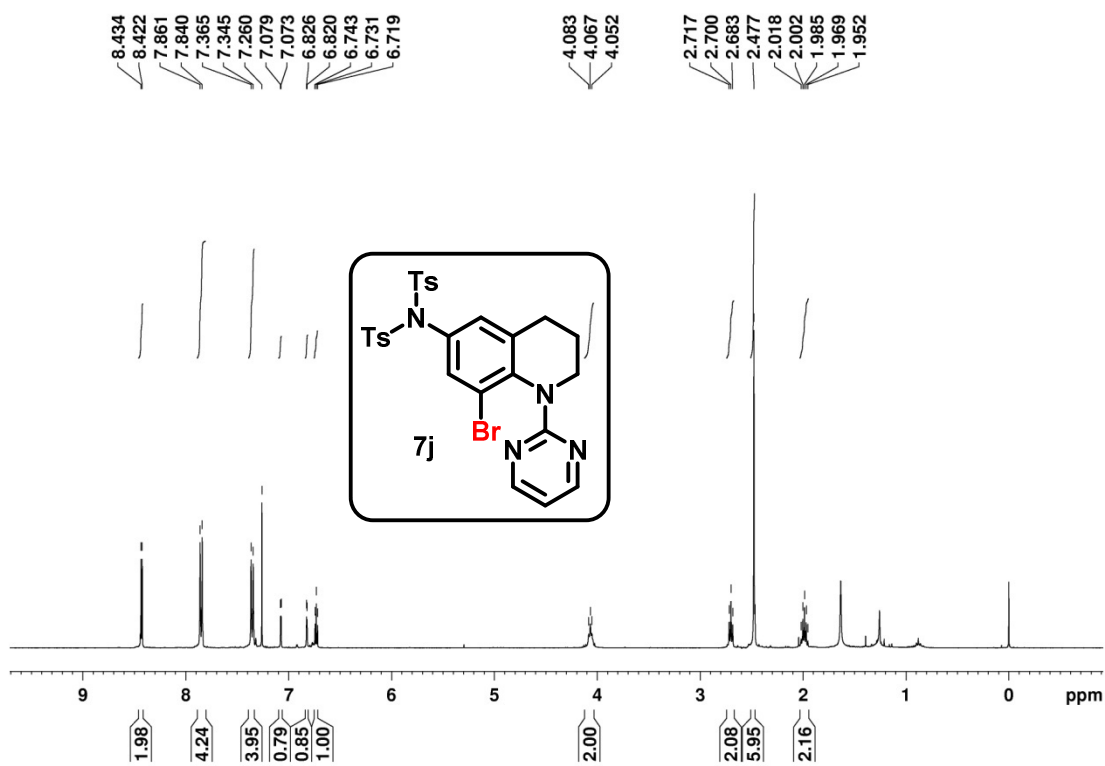


¹H NMR spectrum of **7i** (400 MHz, CDCl₃)

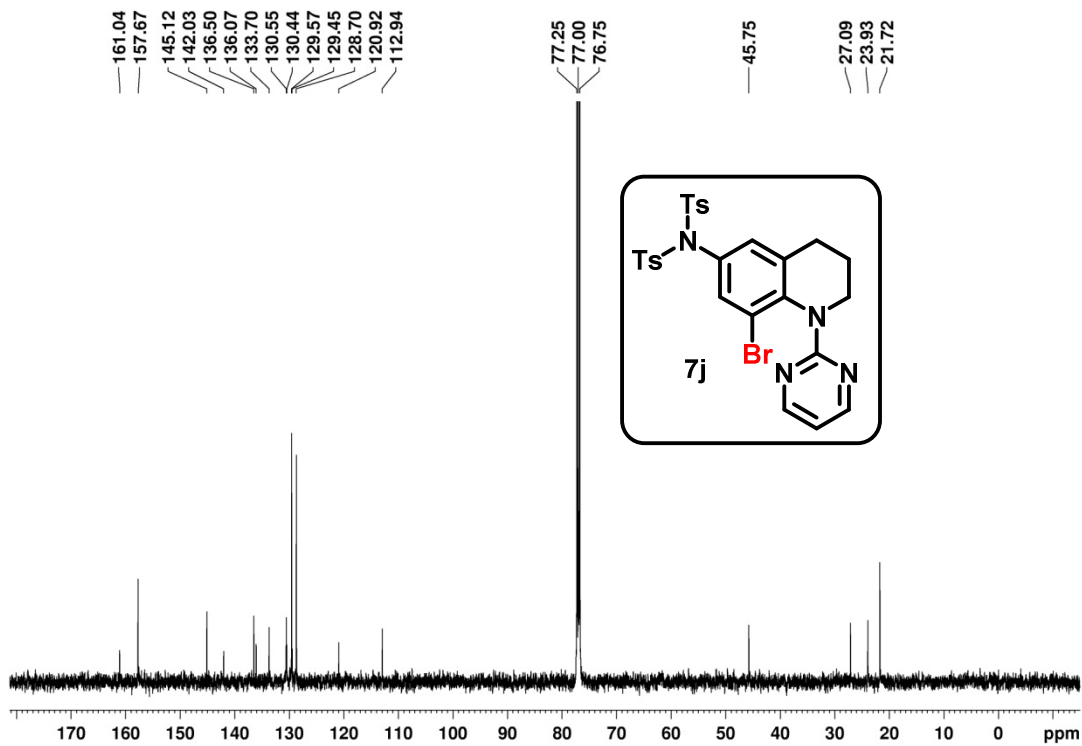


¹³C NMR spectrum of **7i** (100 MHz, CDCl₃)

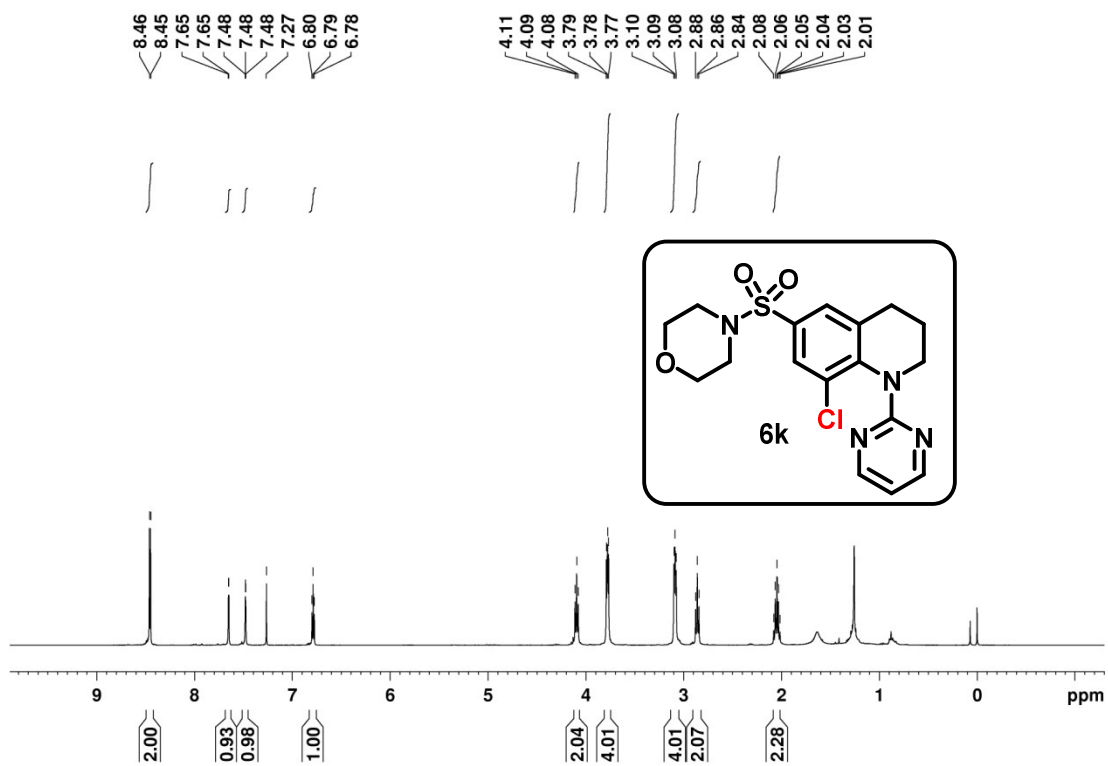




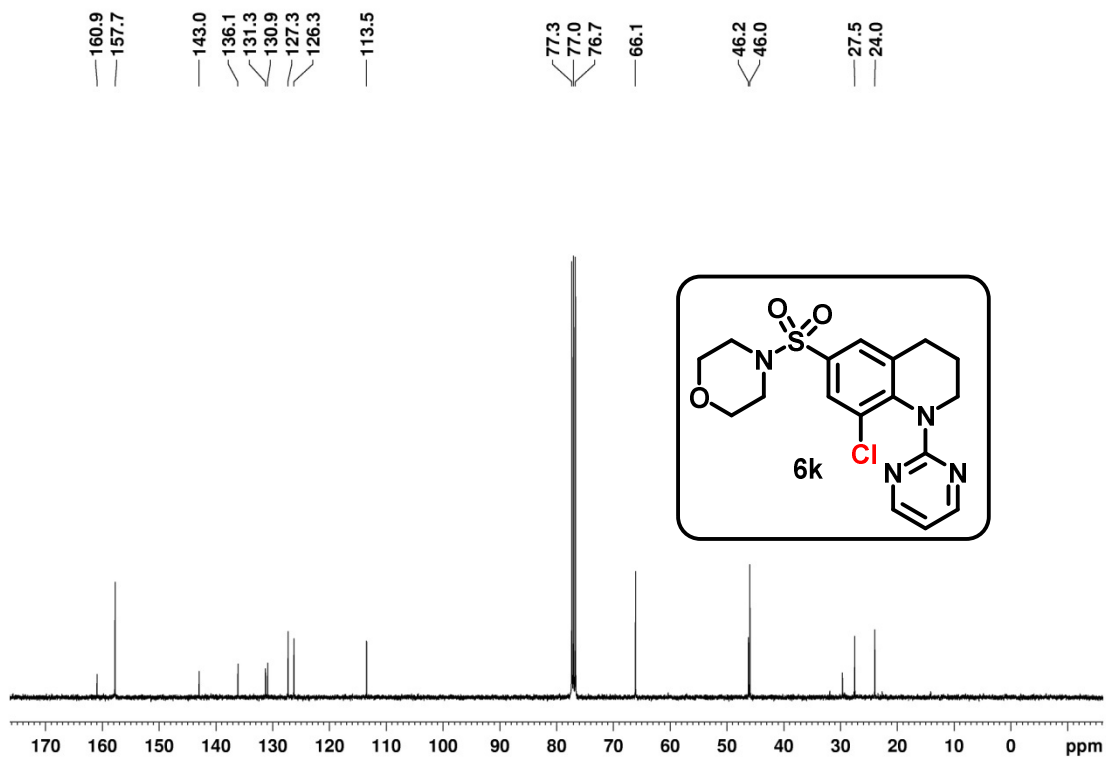
¹H NMR spectrum of **7j** (400 MHz, CDCl₃)



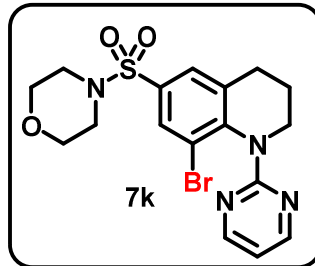
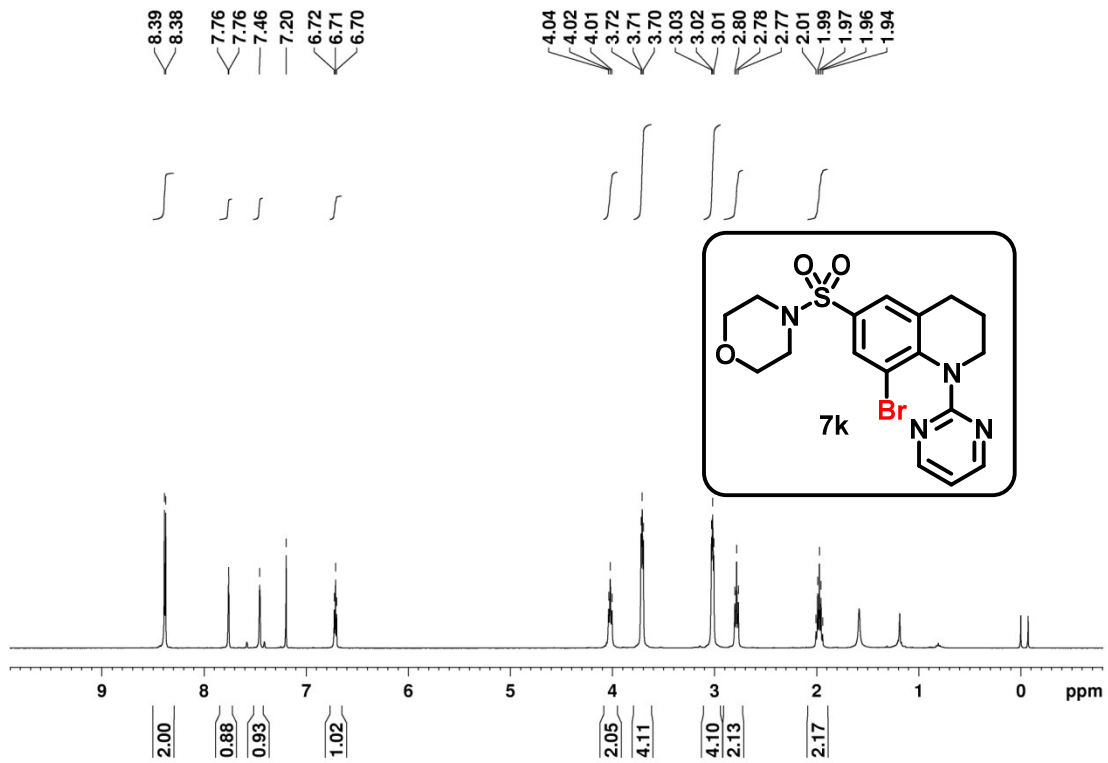
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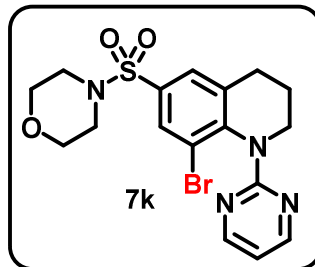
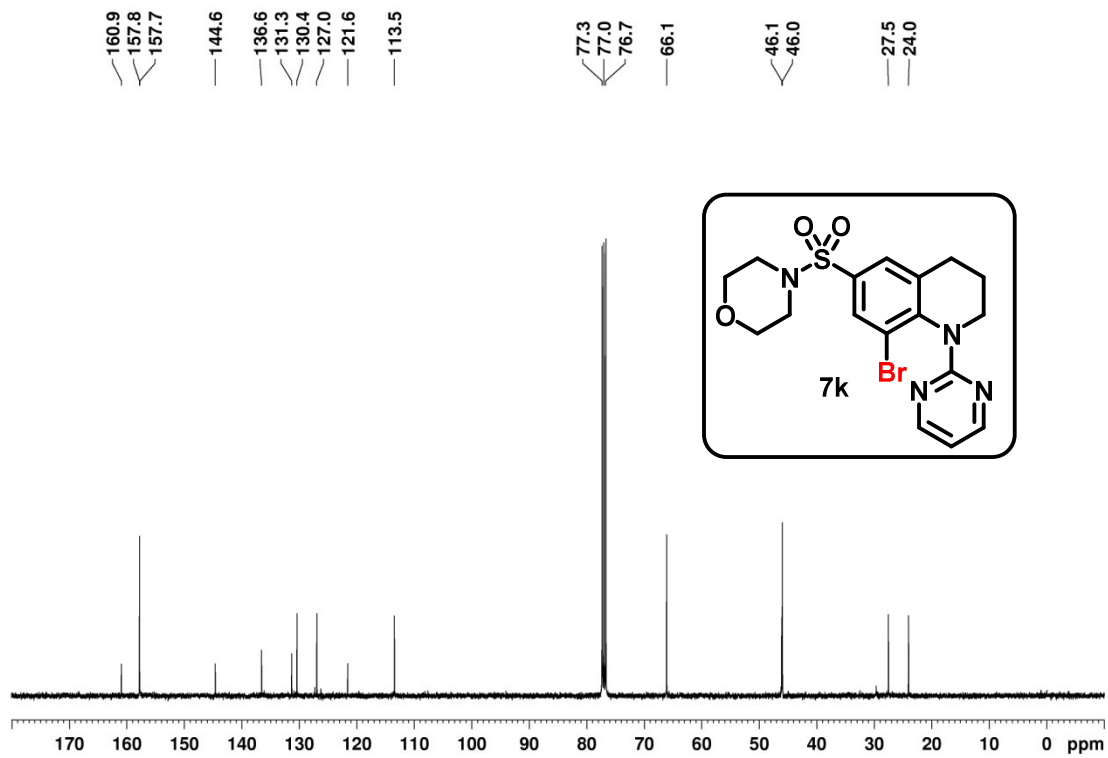
^1H NMR spectrum of **6k** (400 MHz, CDCl_3)



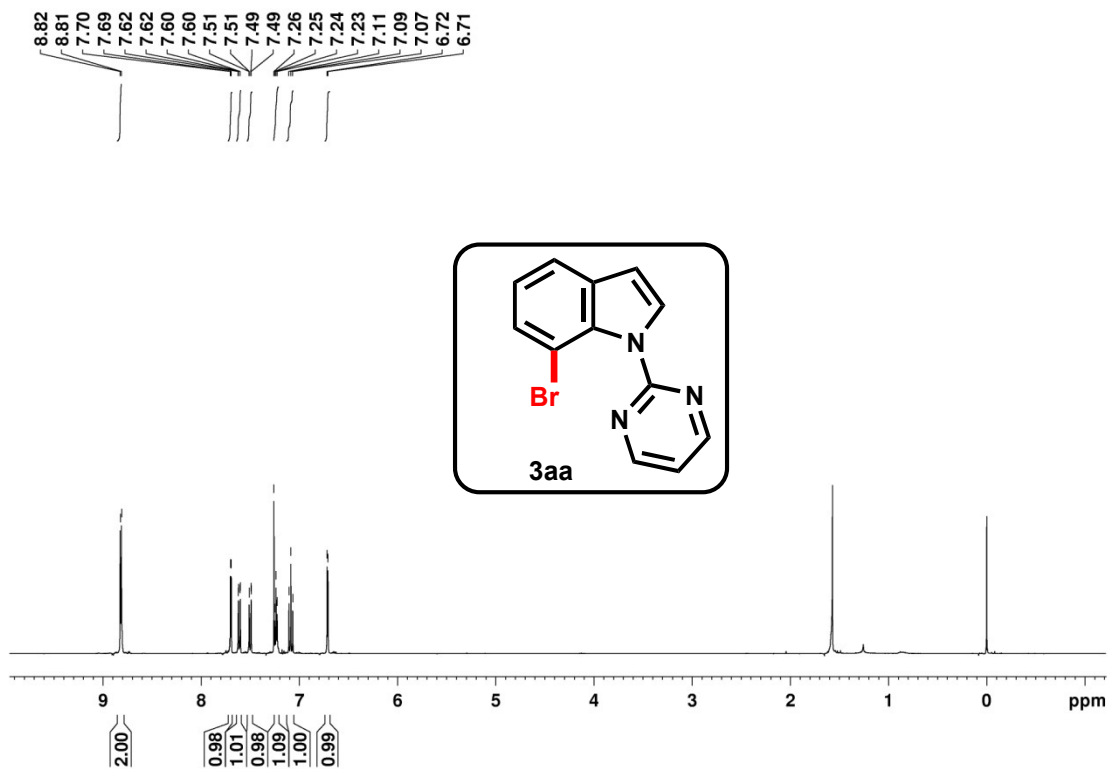
^{13}C NMR spectrum of **6k** (100 MHz, CDCl_3)



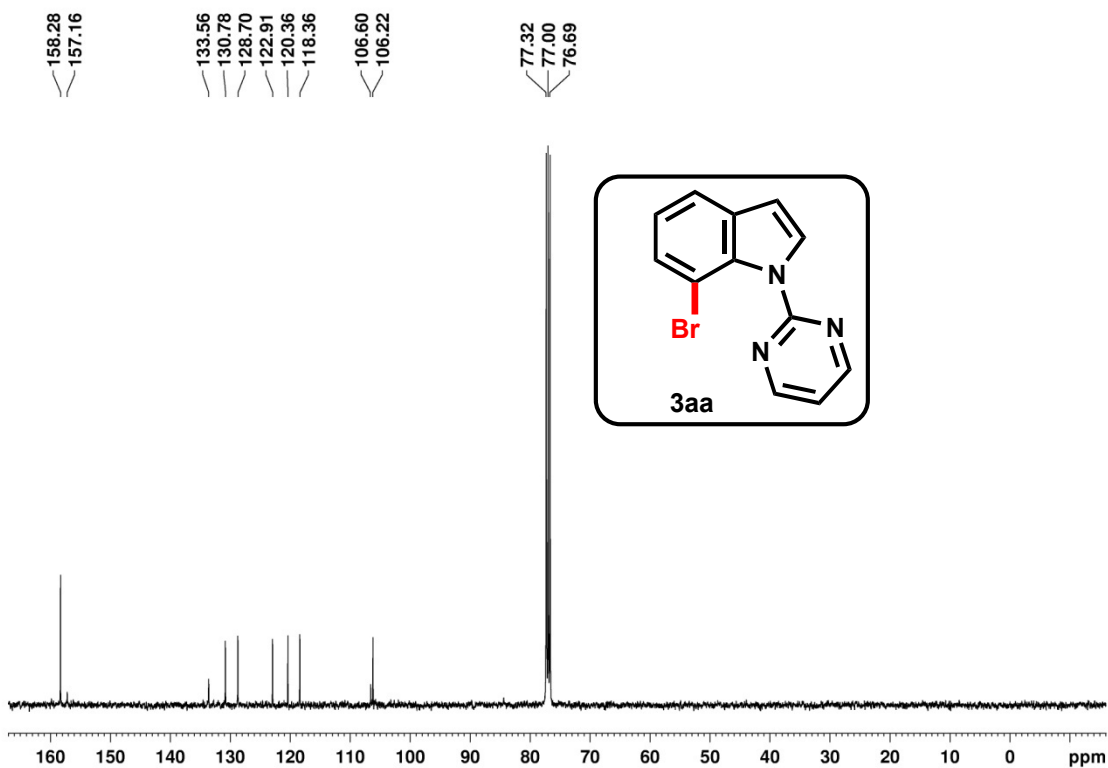
^1H NMR spectrum of **7k** (400 MHz, CDCl_3)



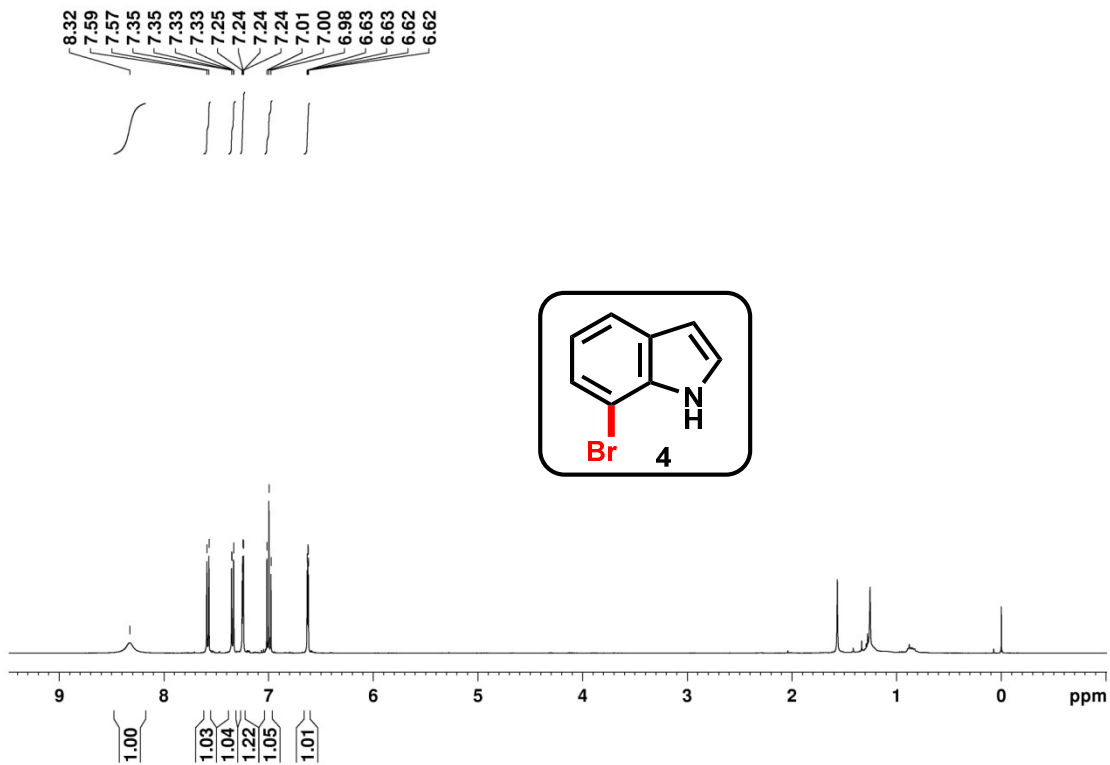
^{13}C NMR spectrum of **7k** (100 MHz, CDCl_3)



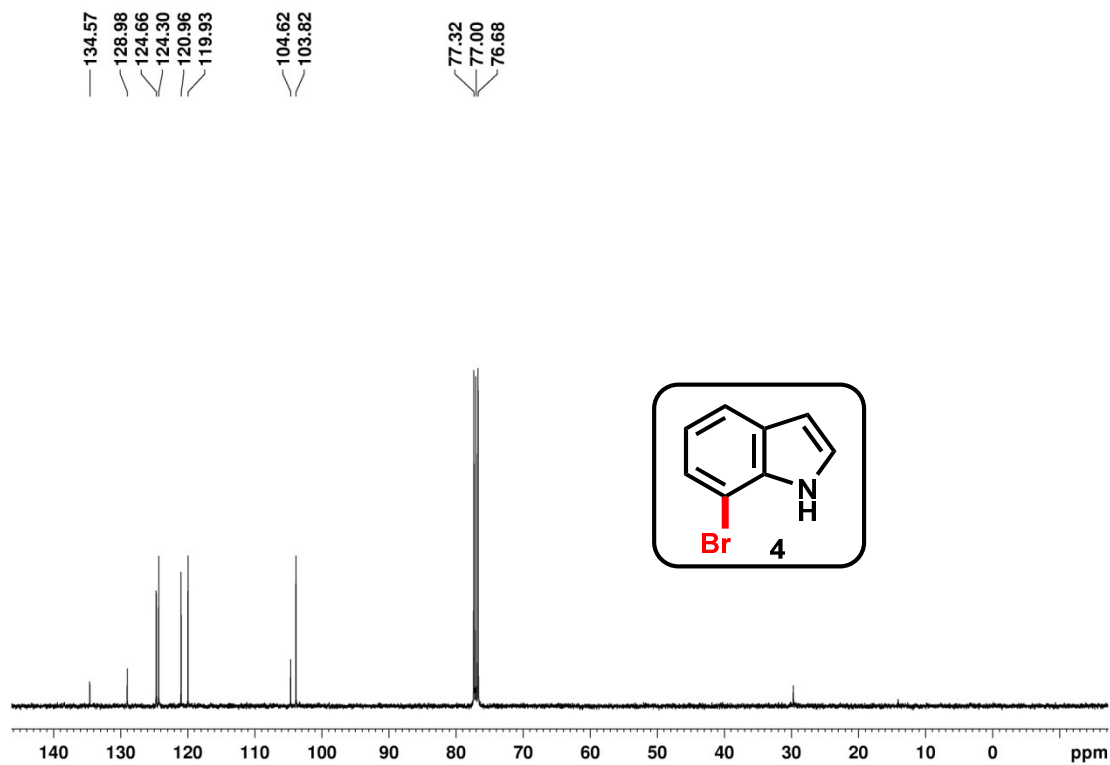
^1H NMR spectrum of **3aa** (400 MHz, CDCl_3)



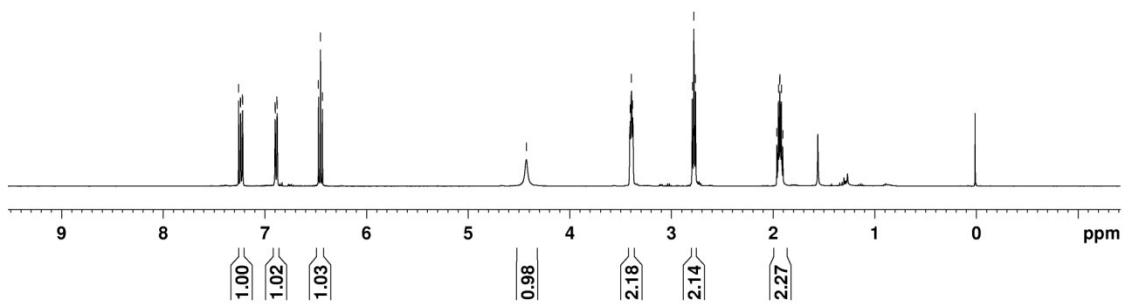
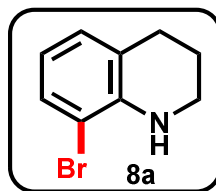
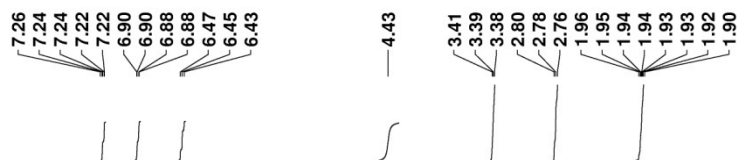
^{13}C NMR spectrum of **3aa** (100 MHz, CDCl_3)



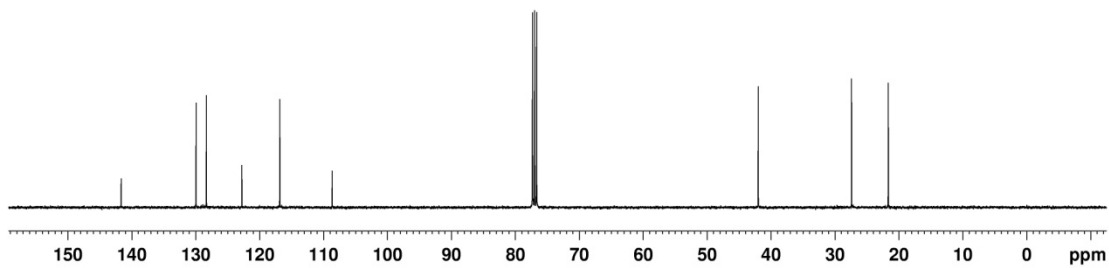
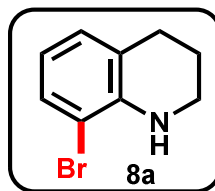
¹H NMR spectrum of 4 (400 MHz, CDCl₃)



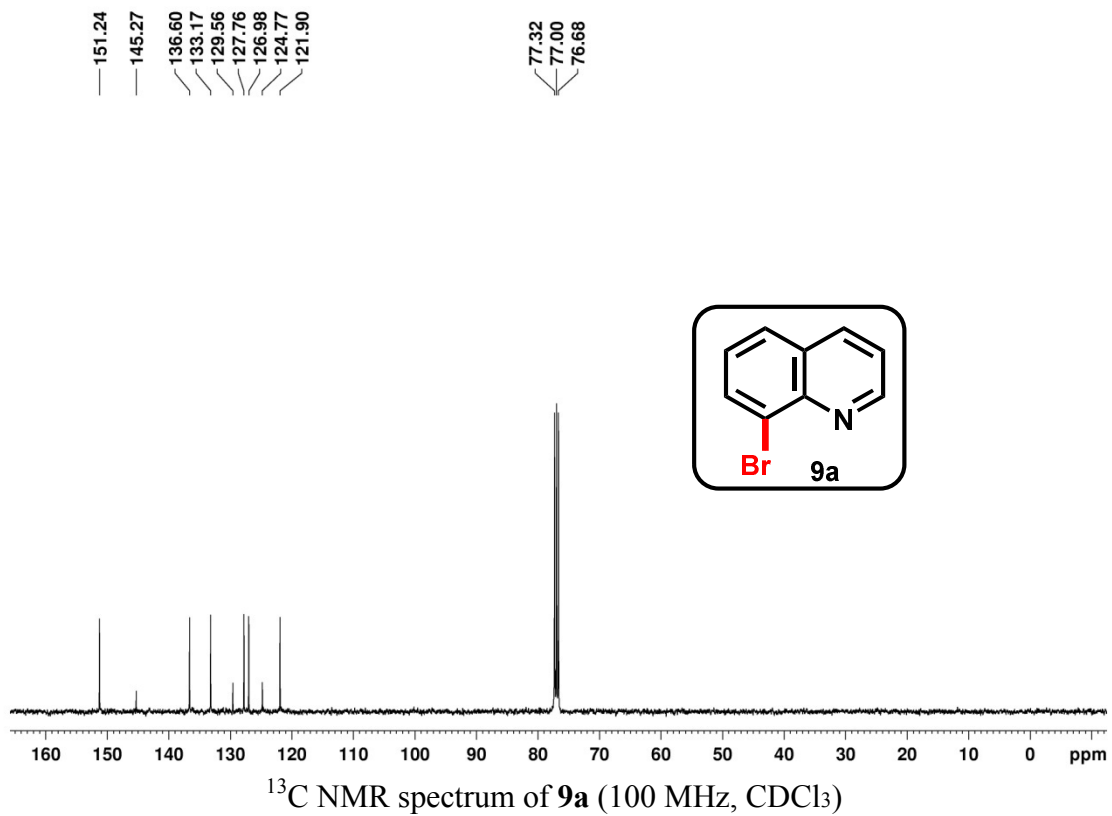
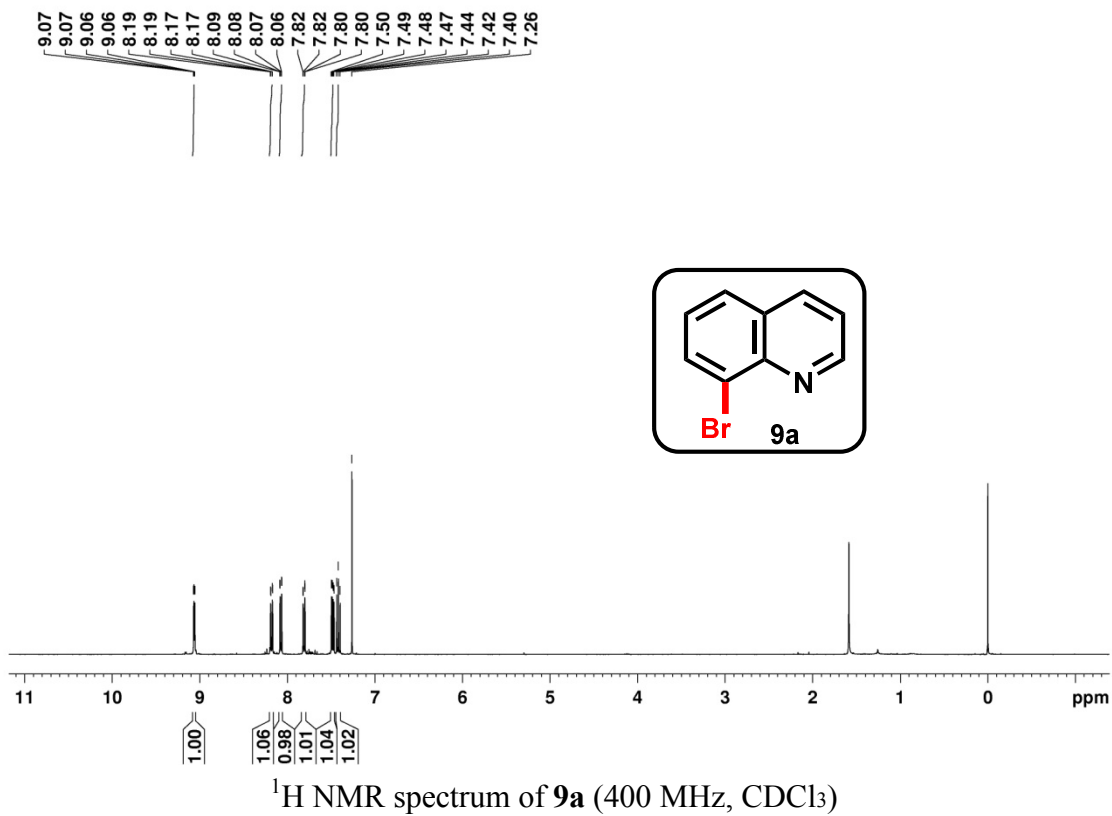
¹³C NMR spectrum of 4 (100 MHz, CDCl₃)

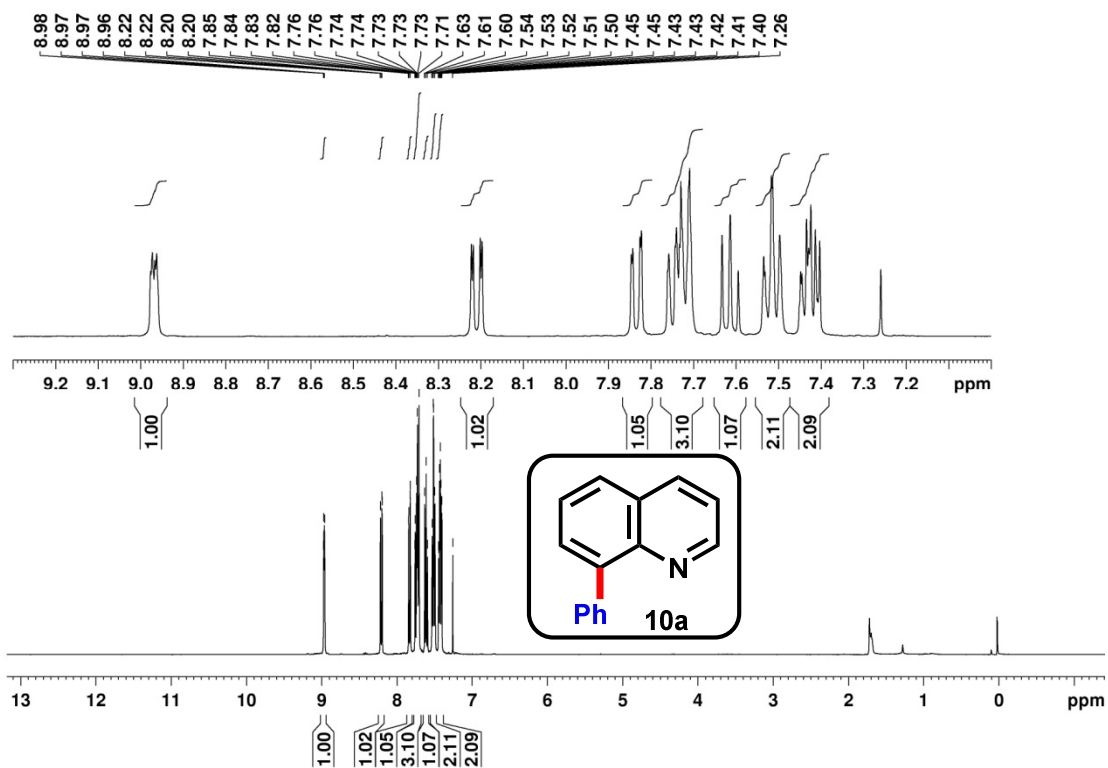


^1H NMR spectrum of **8a** (400 MHz, CDCl_3)

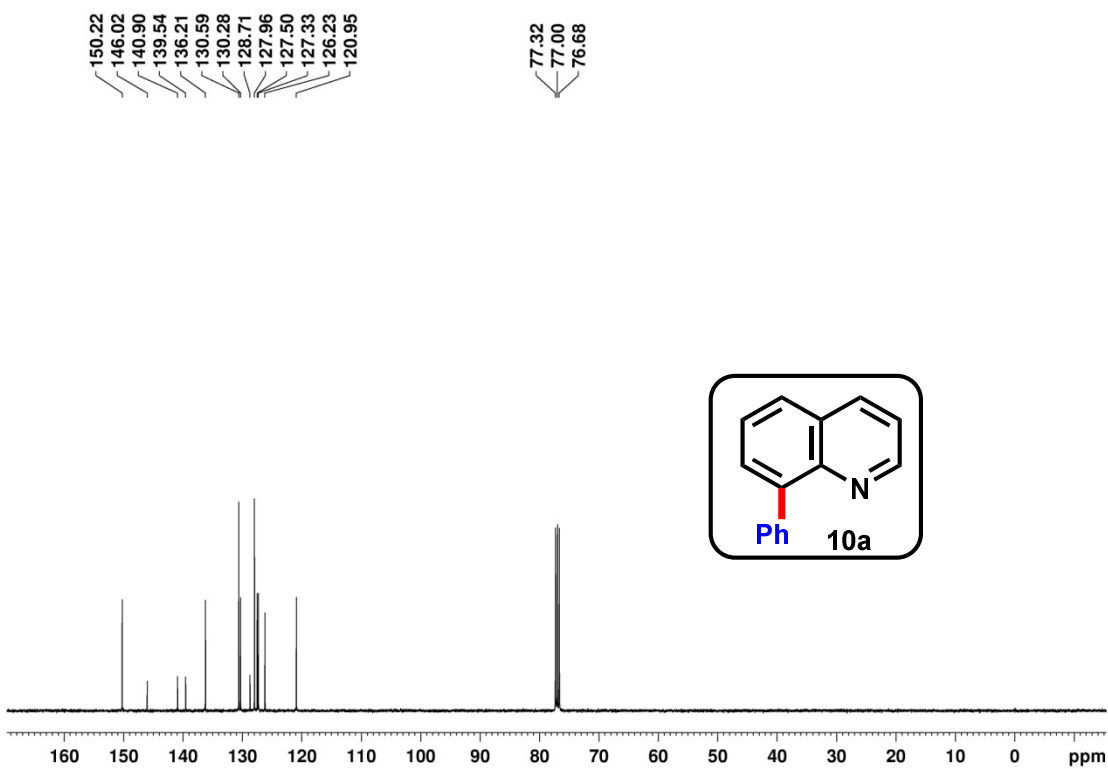


^{13}C NMR spectrum of **8a** (100 MHz, CDCl_3)

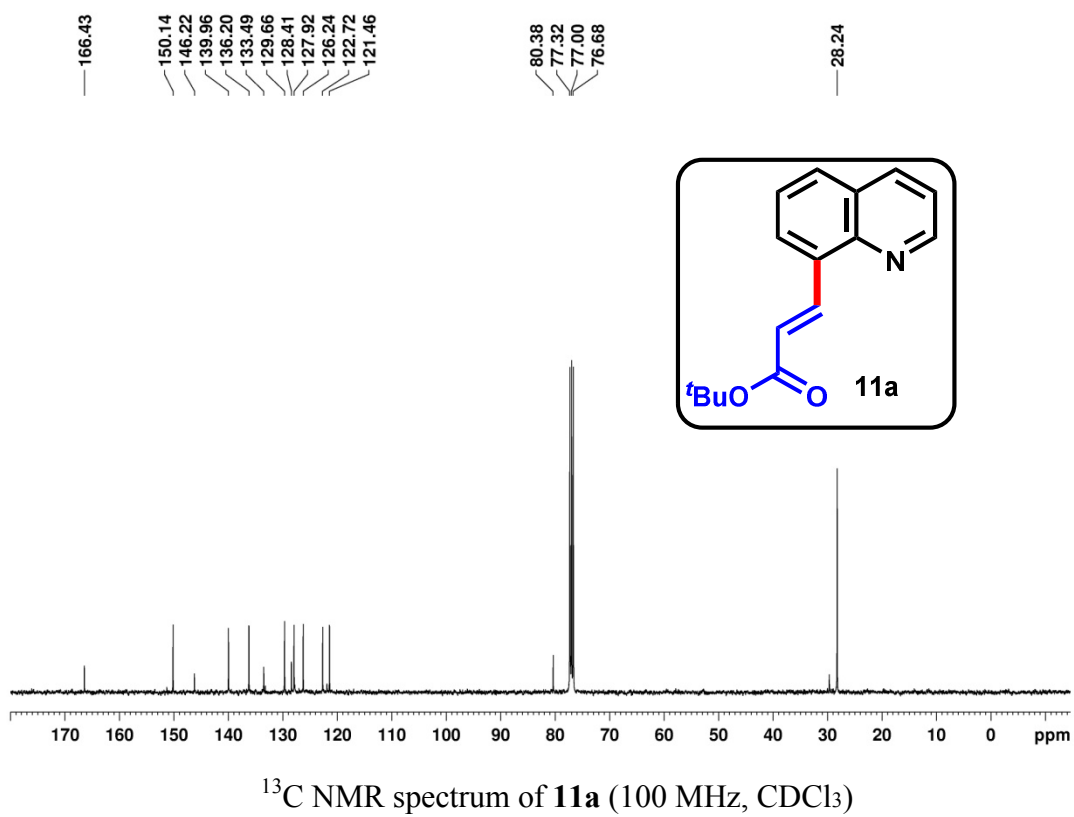
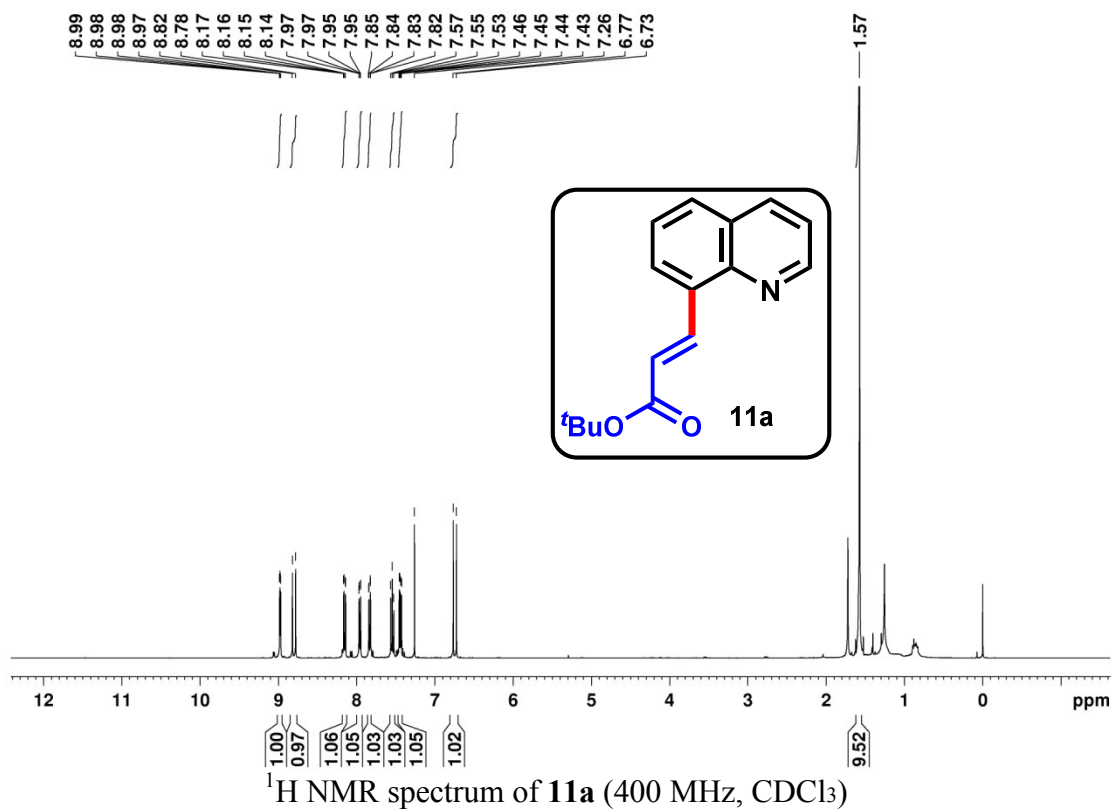


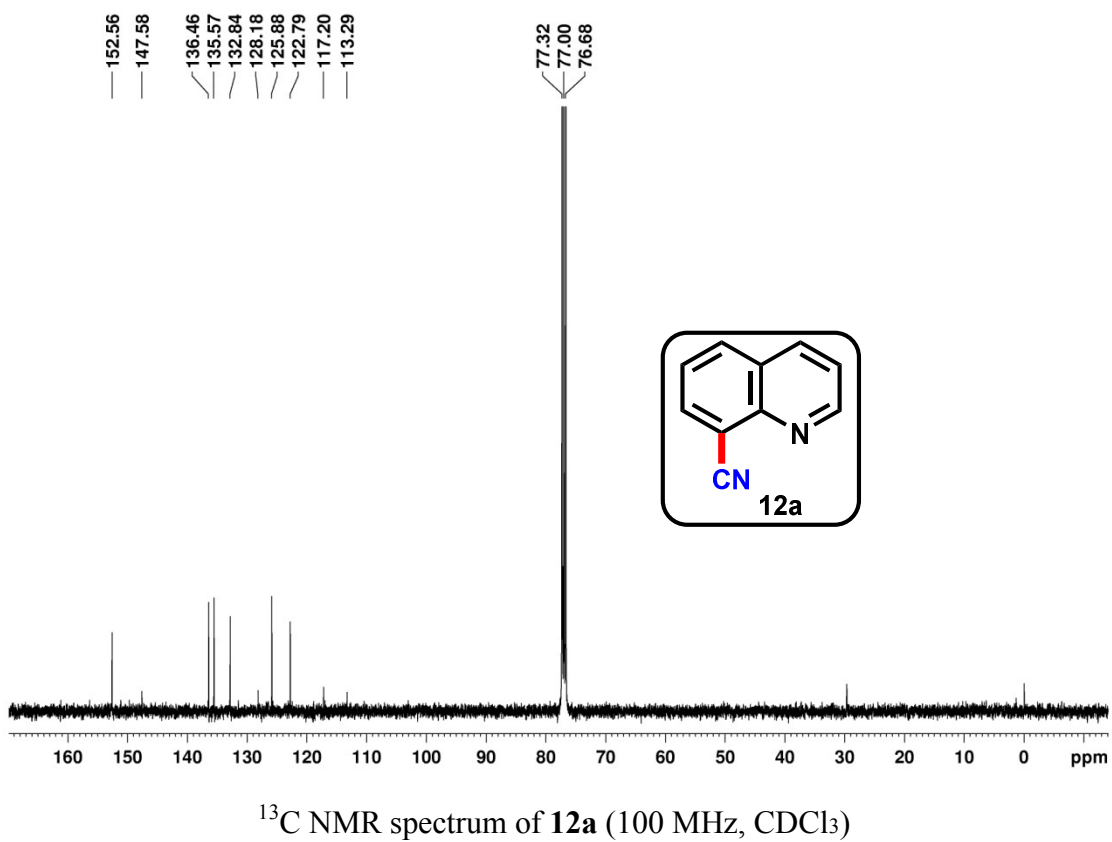
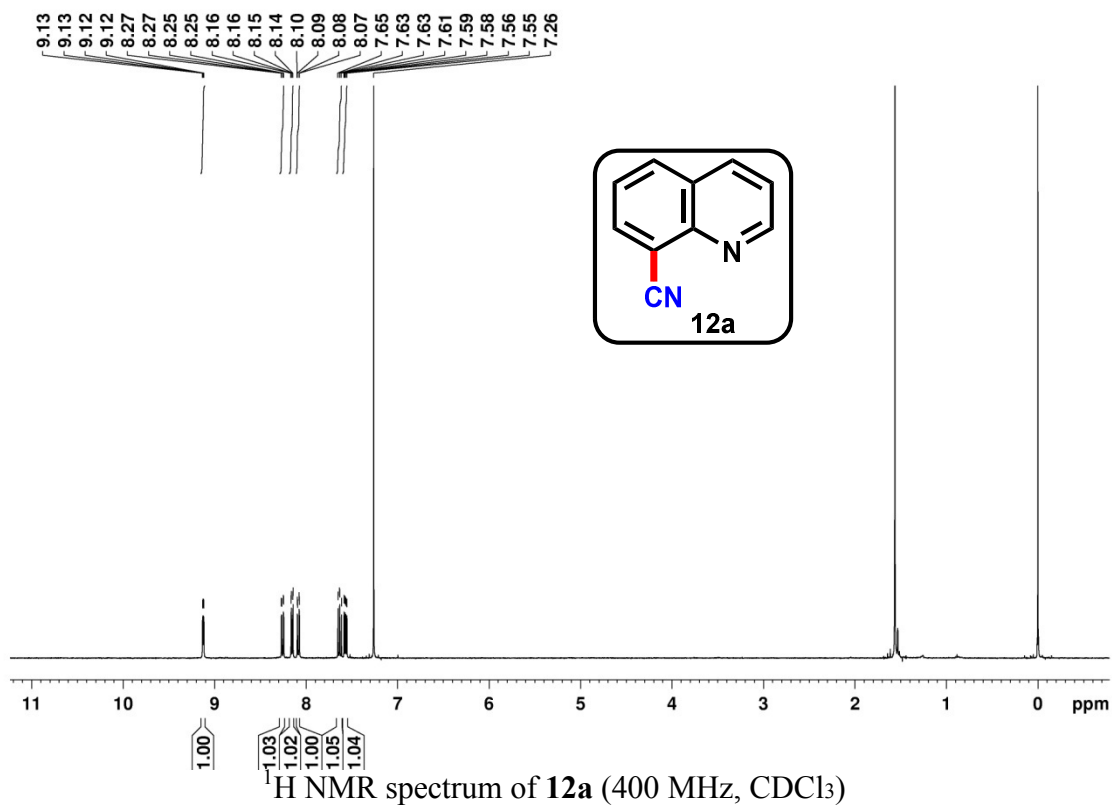


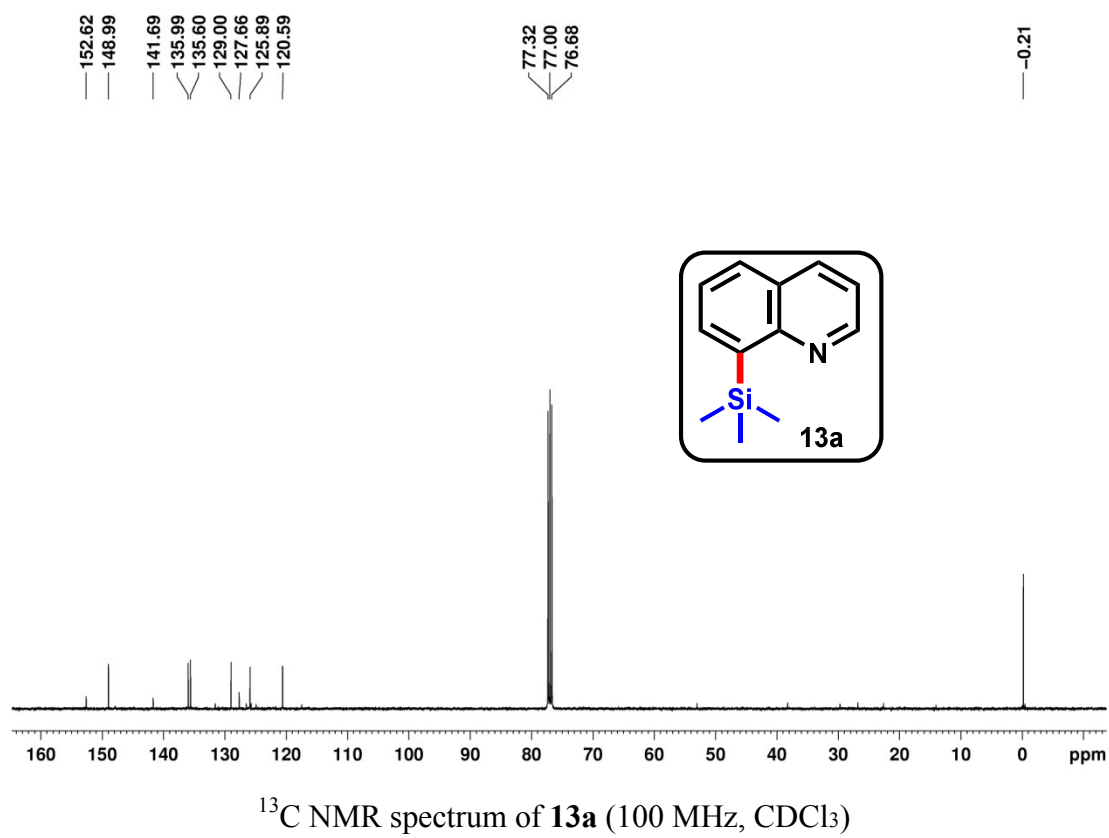
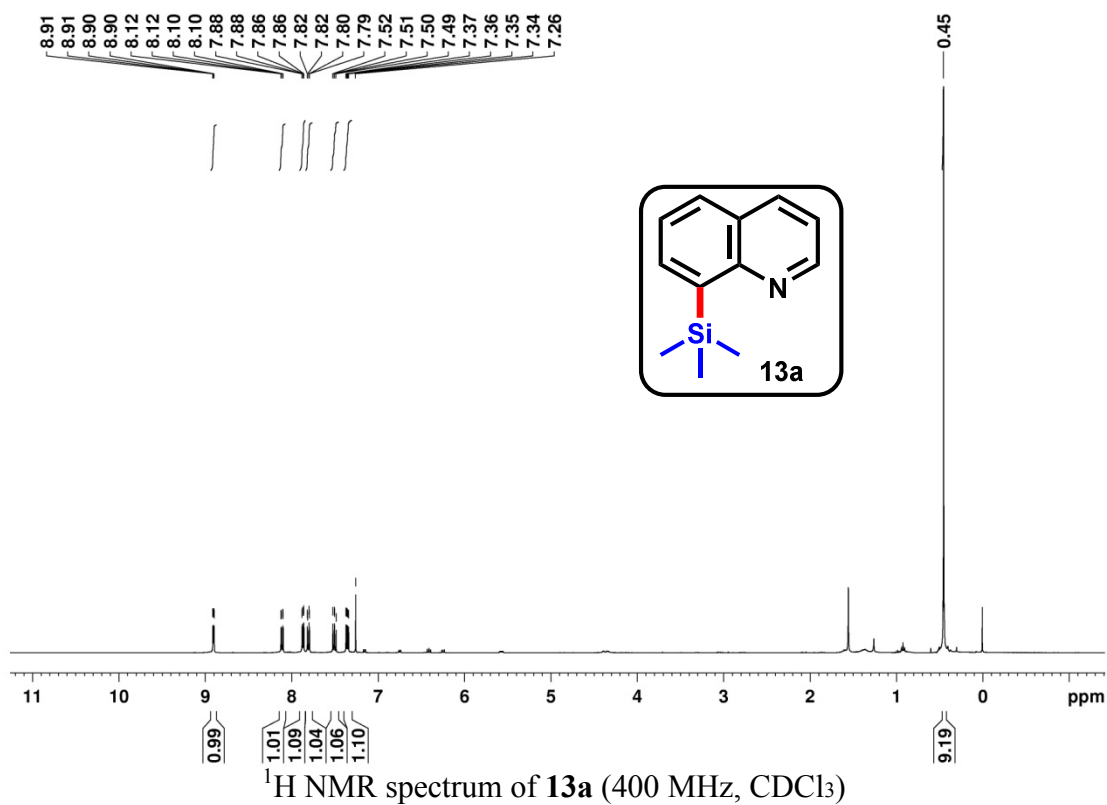
$^1\text{H NMR}$ spectrum of **10a** (400 MHz, CDCl_3)

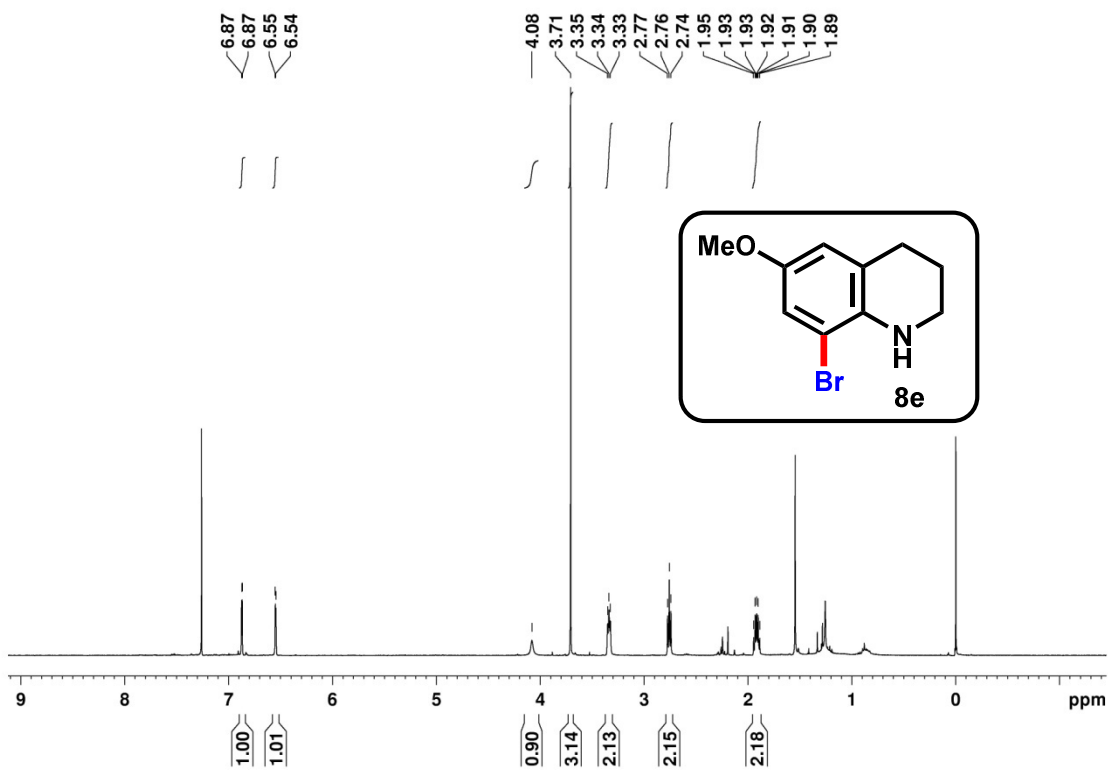


$^{13}\text{C NMR}$ spectrum of **10a** (100 MHz, CDCl_3)

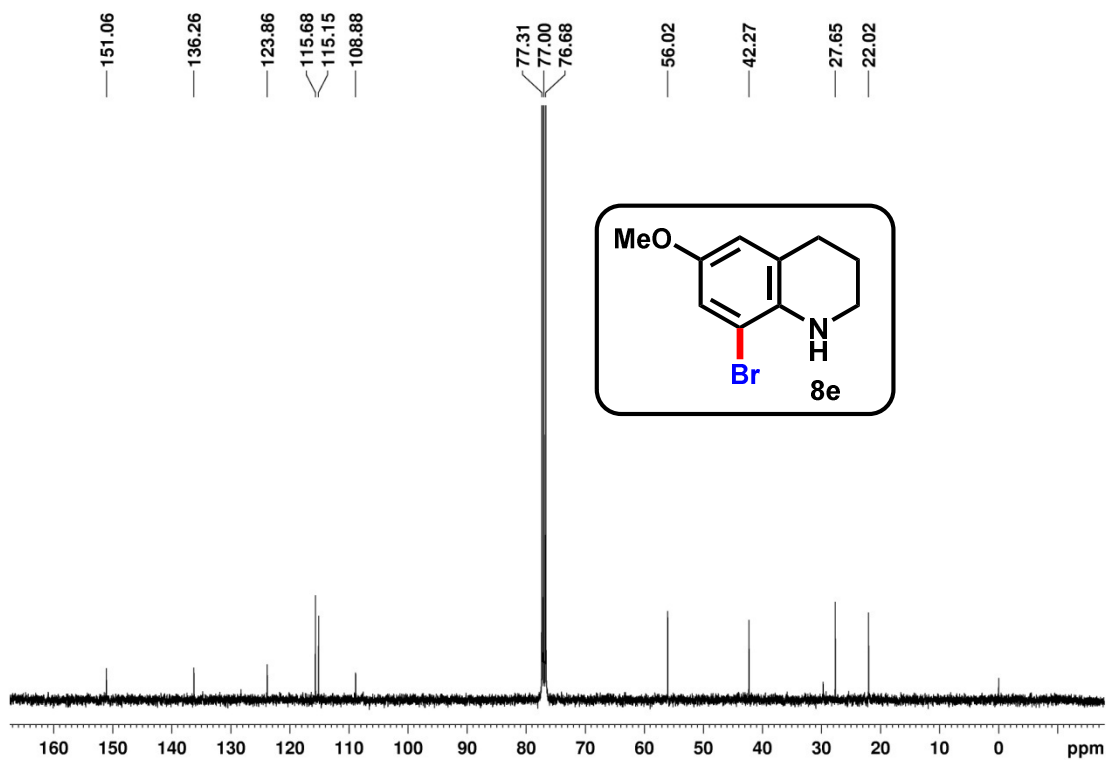




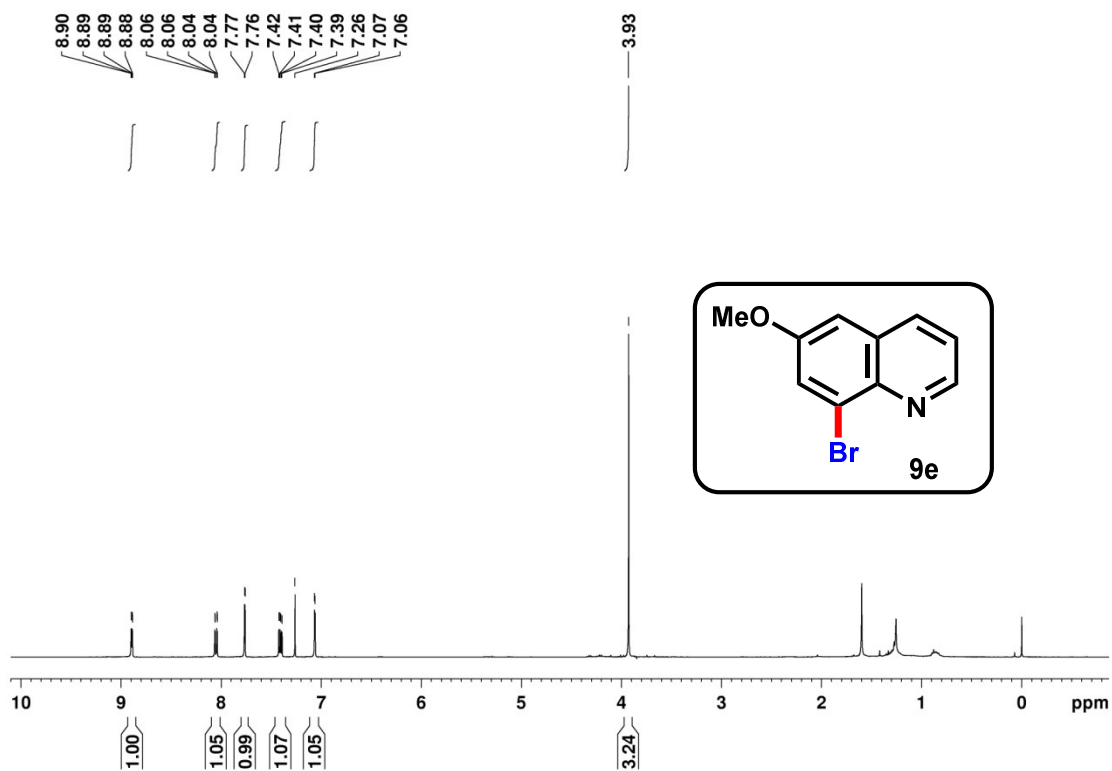




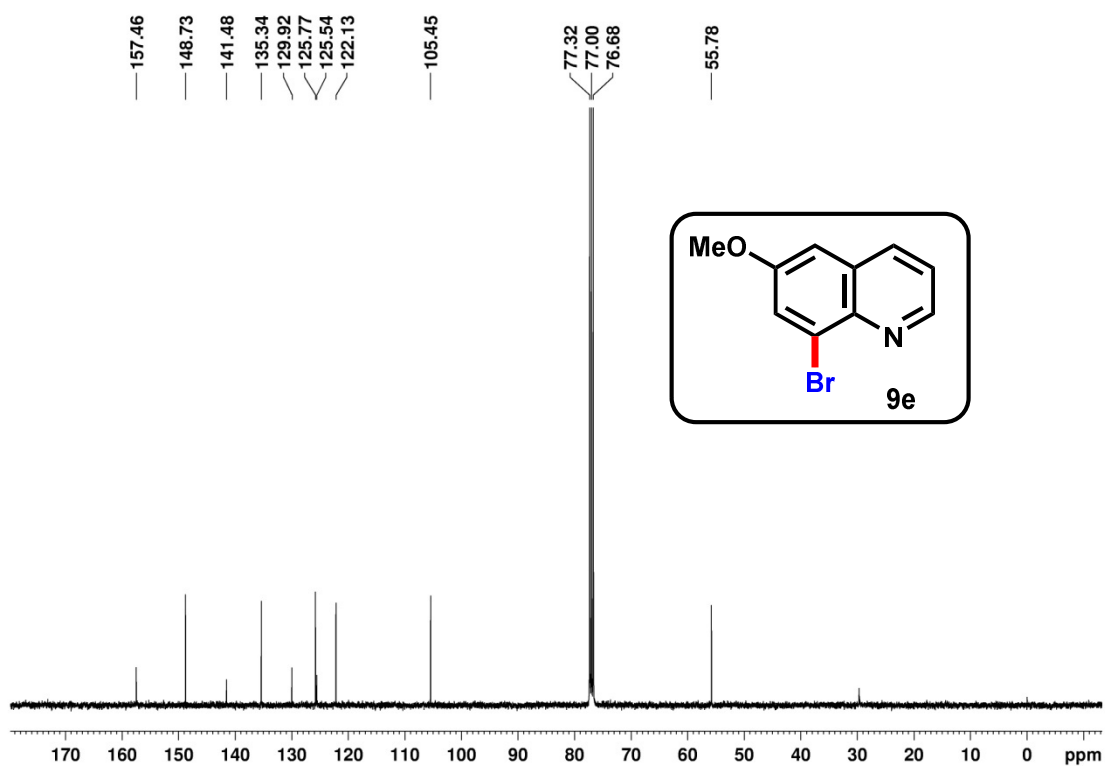
^1H NMR spectrum of **8e** (400 MHz, CDCl_3)



^{13}C NMR spectrum of **8e** (100 MHz, CDCl_3)



^1H NMR spectrum of **9e** (400 MHz, CDCl_3)



^{13}C NMR spectrum of **9e** (100 MHz, CDCl_3)

